

Simplified

PEDIATRICS

(PART TWO)



By

*The Board of Pediatrics Department
Zagazig University*

Arranged by

Dr. Ahmed Galal Siam

MRCPCH-MD

Dr. Mohamed A. Arafa

MD Pediatrics

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②①①⑥

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

(وَوَصَّيْنَا الْإِنْسَانَ بِوَالِدَيْهِ إِحْسَانًا حَمَلَتْهُ أُمُّهُ
كُرْهًا وَوَضَعَتْهُ كُرْهًا وَحَمْلُهُ وَفِصَالُهُ ثَلَاثُونَ
شَهْرًا حَتَّىٰ إِذَا بَلَغَ أَشُدَّهُ وَبَلَغَ أَرْبَعِينَ سَنَةً قَالَ رَبِّ
أَوْزِعْنِي أَنْ أَشْكُرَ نِعْمَتَكَ الَّتِي أَنْعَمْتَ عَلَيَّ وَعَلَىٰ
وَالِدَيَّ وَأَنْ أَعْمَلَ صَالِحًا تَرْضَاهُ وَأَصْلِحْ لِي فِي
دُرِّيَّتِي إِنَّي تُبْتُ إِلَيْكَ وَإِنِّي مِنَ الْمُسْلِمِينَ)

صنق الله العظيم

(الأحقاف: ١٥)

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CHAPTER (I)

HAEMATOLOGY

PHYSIOLOGICAL CONSIDERATIONS

☆ Haematopoiesis:

It means production of RBC's which passes into 3 stages:

- 1- **Yolk sac haematopoiesis:** Primitive RBC's during the first 8 weeks of gestation are formed in the wall of the yolk sac.
- 2- **Visceral haematopoiesis:** From the 2nd month of gestation up to the 6th month some haematopoiesis is present in the spleen, liver, kidney, thymus and lymph nodes.
- 3- **Medullary haematopoiesis:** From the 6th month of gestation, the bone marrow becomes the only site of haematopoiesis and persists till adult life but active marrow (red marrow) in adults will be restricted to skull, vertebrae, sternum & ribs.

☆ Hemoglobin:

◇ Hemoglobin is the unit of RBC's which carry oxygen, it's formed of haeme group (Iron) attached to 2 pairs of polypeptide chains (Protein).



◇ Types of hemoglobin are changed according to the polypeptide chains attached to the heme group:

I- Embryonic hemoglobins: They predominate in Embryo and disappear by the 3rd month of gestation, e.g. Portland and Gower Hb.

II- Fetal hemoglobin: (HbF) predominates during the fetal life and gradually declines till becomes less than 2% at 6-12 months of age → HbF ($\alpha_2 \gamma_2$)

III- Adult hemoglobins:

- Hb A1 (major adult hemoglobin) → $\alpha_2\beta_2$
- Hb A2 (minor adult hemoglobin) → $\alpha_2\delta_2$

- So
- During embryonic life → Embryonic hemoglobins
 - At the 2nd month fetal life → HbF predominate
 - At the 6th month fetal life → HbF 90% & HbA 10%
 - At term → HbF 70% & Hb A 30%
 - At 6-12 month postnatal → HbF <2%, HbA₂ 2-3% & the remaining HbA.

❖ Alteration of the hemoglobins by diseases:

- ◇ Hb A₂ →
 - ↑↑ in B-thalassemia trait and megaloblastic anemia.
 - ↓↓ in α -thalassemia and Iron deficiency anemia.

◇ HbF ↑↑ (>2%) in:

- * Persons with homozygous B thalassemia.
- * 50% of person with heterozygous B thalassemia.
- * Hereditary persistence of fetal hemoglobin.
- * Some cases of sickle cell anemia.
- * Diseases associated with hematological stress e.g leukaemia & pancytopenia.

☆ **Some Blood Indices:**1- **Hemoglobin level:**

- ⊛ 1st 2 weeks of life (16-20 gm %).
- ⊛ Infancy (10-14 gm %).
- ⊛ Adult (14 in female & 16 in male).

2- **RBC's count:**

- ⊛ 6 million/CC in newborn.
- ⊛ 4-5 million/CC after that.

3- **Hematocrite value** (Packed cell volume):

The percentage of RBC's volume in 100 cc blood $\approx$ 40-50.

4- **Mean corpuscular volume (MCV):**

= Mean volume of single red blood cell

(Hematocrite value / RBC's count) $\times$ 10 = 75-90 femtolitre.

- If < 70 = Small RBC's = Microcytes.
- If > 100 = Large RBC's = Macrocytes.

5- **Mean corpuscular hemoglobin (MCH):**

= Amount of hemoglobin in single red blood cell

MCH = (Hb / RBC's count) $\times$ 10 $\approx$ 30 picogram

- If low = hypochromic cells.
- If high = hyperchromic cells

6- **Mean corpuscular hemoglobin concentration (MCHC):**

= Concentration of hemoglobin in single red blood cell.

MCHC = (Hb/Ht value) $\times$ 100 = 33%

7- **WBC's count:**

- In newborn 10000 – 15000 / CC
- After that 5000 – 10000 / CC

8- **Platelet count:**

- 150000 – 400000 / CC

9- **Reticulocytic count:**

- In newborn $< 5\%$
- After that $< 2\%$

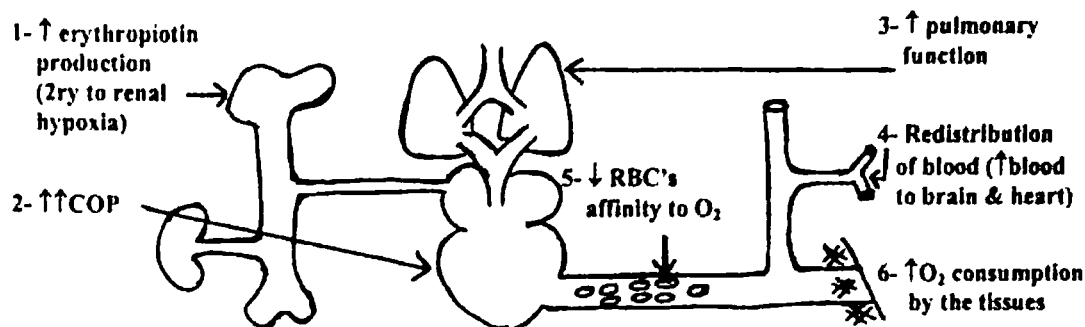
ANEMIA

☆ Definition:

A condition in which the concentration of hemoglobin or the number of RBC's are reduced below normal values for age and sex.

☆ Compensatory mechanisms:

Before anemia becomes manifest and clinical presentation of reduced oxygen to the body organs occur, the body will respond to the hypoxia (reduced oxygen) by:-



✧ If compensatory mechanisms fail to correct ↓ O₂ manifestations of anemia occur:

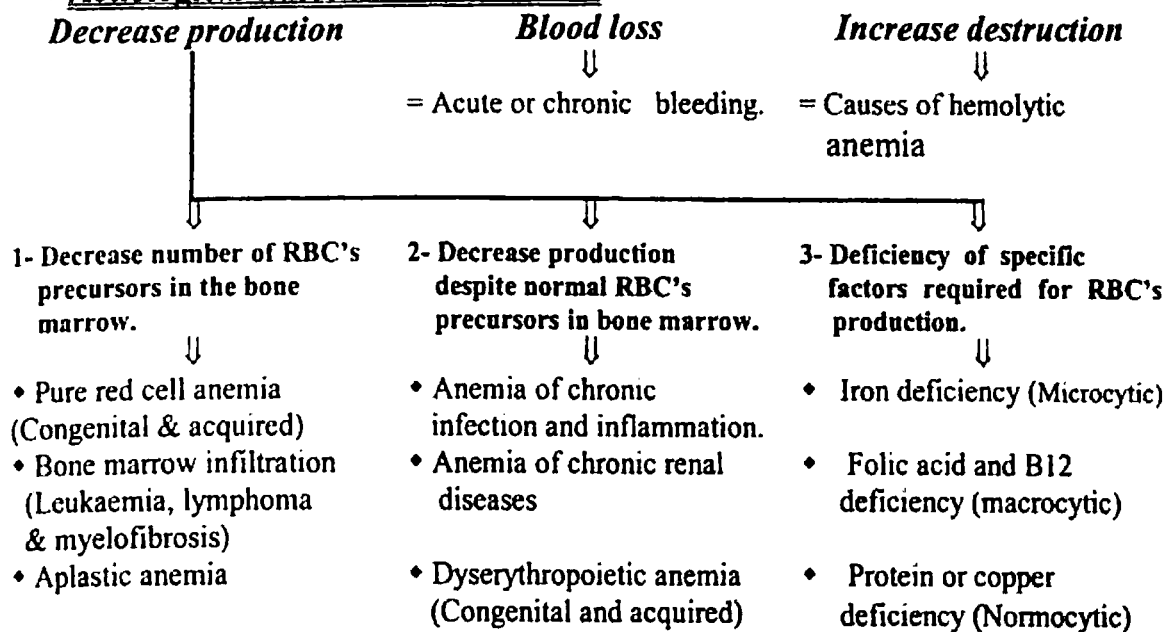
Symptoms:

- ♦ Anorexia, loss of weight, restlessness and easy fatigability.
- ♦ Later on headache, fainting, anginal pain and intermittent claudications.

Signs:

- ♦ Pallor (the most important sign).
- ♦ Hemic murmurs (functional, systolic), tachycardia & anemic HF in severe cases.

☆ Aetiological classification of anemia



☆ Morphological classification of anemia

- 1- Microcytic hypochromic anemia
- 2- Macrocytic anemia.
- 3- Normocytic anemia.

A- Anemia resulting from ↓↓ RBC's precursors in bone marrow

I- Pure red cell anemia: (hypoplastic anemia)

The precursors of RBC's only in the bone marrow are decreased or absent:

1- Congenital pure red cell anemia (Diamond Blackfan S.)

familial disease of unknown cause chch by anemia(by 2- 6 months), and associated

congenital anomalies e.g. triphalangial thumb.

▣ **Lab:** ↓ RBC's, normal platelets and WBC's, ↓ retics and ↑ Hb F.

▣ **TTT:** corticosteroids → If no response repeated blood transfusion.

2- Acquired pure red cell anemia:

i - Immune disease against RBC's precursors.

ii - Idiosyncrasy to chloramphenicol

iii- Infection with Parvovirus

II. Bone marrow infiltration:

Leukaemia, Myelofibrosis or lymphoma may invade the bone marrow and replace the stem cells resulting in:

- ↓↓ RBC's precursors → hypoplastic anemia
- or ↓↓ Megakaryocytes → thrombocytopenia
- or ↓↓ WBC's precursors → leukopenia
- or ↓↓ All elements of blood = pancytopenia

III- Aplastic anemia:

☆ **Def.** Absence or deficiency of the 3 elements of Bone marrow.

☆ **Causes:**

- ◇ **Congenital:** 1- Fanconi anemia.
- 2- Familial aplastic anemia.

- ◇ **Acquired:** 1- **Idiopathic (70%):** Unknown cause
- 2- **Secondary (30%):**
 - ◇ Chemicals: insecticides, war gases.
 - ◇ Viruses: e.g. Hepatitis, CMV & EBV.
 - ◇ Irradiation.
 - ◇ Drugs:
 - ◆ Antineoplastic → Endoxan, methotrexate, 6MP.
 - ◆ Antibiotics → Sulpha, nitrofurantion, chloramphenicol.
 - ◆ Anticonvulsants → Hydantoin, carbamazepine
 - ◆ Anti-inflammatory → Indomethacin, phenylbutazon.
 - ◆ Antimalarial → Chloroquine
 - ◆ Antithyroid → Carbimazol, propylthiouracil.

☆ **Clinical picture:**

- 1- **Anemia:** Pallor & other manifestations of anemia.
- 2- **Leukopenia:** Recurrent infection
- 3- **Thrombocytopenia:** Purpura, bleeding
- 4- **No organomegaly** (liver, spleen, LN)
- 5- **Features of the cause:**
 - δ Fanconi anemia (AR) is chch by:
 - ♦ Variable onset of anemia (4-12 yrs old)
 - ♦ Skin pigmentation, short stature, skeletal anomalies (abnormal thumb, absent radius, skull anomalies,).
 - ♦ MR in 20 % of cases.
 - δ History of drug, irradiation or chemical exposure in 2ry aplastic anemia.

☆ **Investigations:**

- ❖ Blood → Pancytopenia (Also ↓ reticulocytes) + macrocytic RBC's.
- ❖ Bone Marrow → hypocellularity of all 3 elements
- ❖ In Fanconi → ↑ chromosomal breakage (>20- 70%)

☆ **D.D.:**

- Other causes of pancytopenia: ♦ Hypersplenism
 - ♦ Bone Marrow infiltration
 - ♦ Megaloblastic anemia
- Other causes of macrocytic anemia: see later

☆ **Treatment:**

- 1- **Supportive care:**
 - ❖ TTT of anemia (packed RBC' s transfusion if Hb < 7 gm / dl).
 - ❖ TTT of bleeding (avoid IM injection / fresh frozen plasma).
 - ❖ TTT of infection (antibiotics / isolation / G-CSF).
- 2- **Specific ttt:**
 - ❖ Immunosuppressives (corticosteroids, cyclosporin A & antithymocyte globulin).
 - ❖ IV gamma globulins
 - ❖ Bone marrow transplantation

B- Iron deficiency anemia

☆ Iron metabolism.

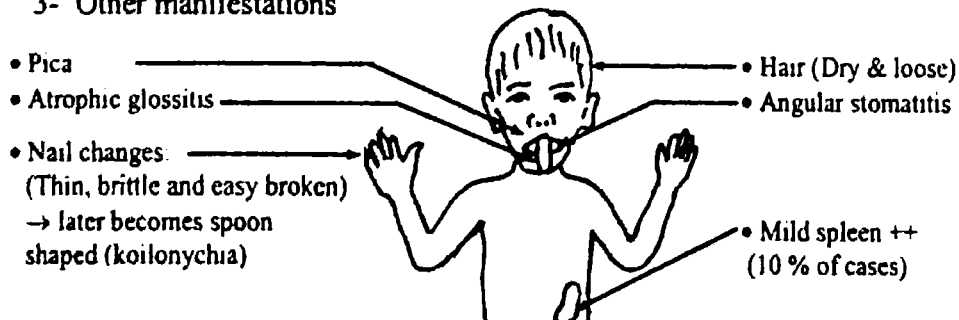
- ❖ Most of dietary iron is present in ferric state, which is released & changed to ferrous state by the combined action of HCL and Vit. C. then absorption occurs from the proximal small intestine (about 10% of dietary iron is absorbed only). The absorbed iron is carried on plasma protein called transferrin, the transferrin can carry 3 times than average of plasma iron when it's said to be fully saturated. So, TIBC (Total iron binding capacity) $\approx$ 300-400 ug/dl.
- ❖ Normal serum iron is 60-120 ug/dl
- ❖ Daily requirements of iron is about 1 mg daily & as 10% only of dietary iron is absorbed so the daily diet must contain 10mg iron
- ❖ Functions of iron:
 - ♦ Formation of hemoglobin in RBC's
 - ♦ Essential in certain enzymes necessary for body functions as catalase, MAO, ...

☆ Aetiology:

- 1- Intake: Exclusive breast feeding or unfortified powdered milk without supplementation is important cause of anemia at 6-9 months of age (after exhaustion of transplacental iron stores)
- 2- Absorption: in malabsorption or excess intake of tea, antacids,
- 3- Chronic blood loss:
 - ♦ Ankylostoma duodenale
 - ♦ Cow's milk protein allergy
 - ♦ Peptic ulcer, piles, Meckel's diverticulum,...
 - ♦ Frequent blood sampling in neonates
- 4- Increased demand:
 - ♦ Increased growth rate in premature and adolescents.
 - ♦ Cyanotic CHD.

☆ Clinical Manifestations:

- 1- General manifestations of anemia.
- 2- Manifestations of enzymes deficiency (Defective alertness, learning & concentration)
- 3- Other manifestations



☆ Investigations:

1. Hypochromic Microcytic Anemia
 ↓ ↓ ↓
 MCH < 30 Pg MCV < 70 fl Hb ↓, RBC's ↓, ↓ MCHC, ↑ RDW
2. Serum iron ↓↓ (N. 60–120 µg/dl)
 3. TIBC ↑↑ (N. 300–400 µg/dl)
 4. Serum ferritin ↓↓ (reflecting iron stores)
 5. Transferrin receptors ↑↑.
 6. For the cause e.g. stool analysis for ankylostoma.

☆ Differential diagnosis:

Causes of Hypochromic microcytic anemia:

Cause	Serum Fe	TIBC	Other investigations	N.B
1 Iron ↓ anemia	↓↓	↑↑	- Stool for occult blood & ankylostoma	The commonest cause
2. Anemia of chronic diseases	↓↓	↓↓	- For the cause (chronic diseases)	Usually normocytic, occasionally hypochromic microcytic
3. Sideroblastic anemia	Normal or ↑↑	Normal or ↓↓	- Sideroblasts in blood	Abnormality in haeme metabolism either cong. or acq., may respond to Vit. B6
4 Lead poisoning	Normal	Normal	- Basophilic stippling of RBC's & ↑ lead level in the blood.	History of exposure to lead ± blue lines on gums
5. β-Thalassemia	Normal or ↑↑	Normal or ↓↓	- Reticulocytosis - ↑ HbA ₂ - ↑ HbF	(Hemolytic microcytic anemia)

N.B. ☞ Mentzer index = $\frac{\text{MCV}}{\text{RBC's count}}$ (If < 13 → β - thalassemia trait, if > 13 → Fe ↓)

☆ **Treatment of iron deficiency anemia:**

1. **Prophylactic:** Oral iron preparations are given after the 3rd month (2mg/kg/day)

2- **Treatment:**

a- Causal treatment (e.g. Ankylostoma, Mickle's, ...).

b- ♦ Oral iron preparations (6mg/kg/day)
♦ Parenteral iron in severe vomiting
♦ Iron rich foods

} For 4-6 weeks after return of indices to normal (to fill iron stores).

c. Blood transfusion: In severe cases or anaemic H.F.

3- **Criteria of improvement:**

a- ↑ appetite and ↓ irritability (within one day)

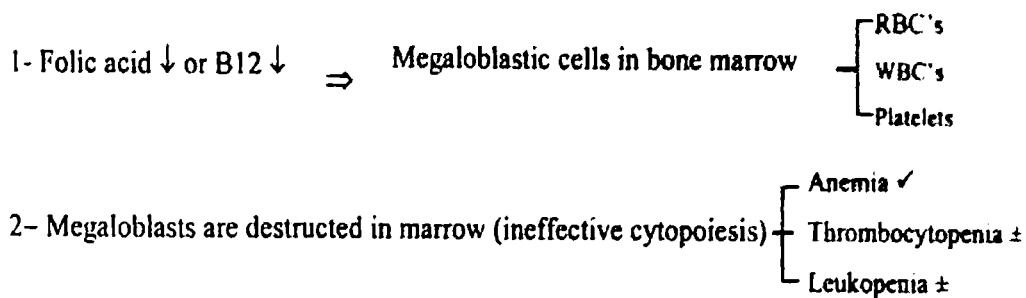
b- ↑ reticulocytic count (within one week)

c- ↑ Hb to normal values (within one month).

C- Megaloblastic Anemia

☆ Pathogenesis of megaloblastic anemia:

- ❖ Megaloblastic is a term denoting abnormal cell production in which ↓DNA formation occurs with normal RNA, as a result the nucleus becomes smaller in relation to large cytoplasm (Nucleo- Cytoplasmic Dissociation)
- ❖ Megaloblastic anemia is anemia resulting from folic acid or vit. B12 deficiency which are essential substances for DNA production resulting in megaloblastic changes not only in RBC's but WBC's and Platelets may be also affected:



Metabolism of Vit. B12	Folic acid
Sources: Animal origin only (milk, Meat, seafood, Liver)	⇒ -Animal (liver, Kidney) -Plant (green leaves, fruits)
Requirements: 5-20 µg/day. Body stores sufficient for 5 yrs	⇒ 20-60 µg/day. Body Store are much less than B12
Function: Methyl malonic acid $\xrightarrow{\text{B12}}$ succenyl CoA	⇒ Histidine → Formiminoglutamic acid (FIGLU) — Folic Acid → Glutamic acid
Absorption: Stomach parietal cells release Intrinsic factor (IF) which bind to B12 till absorbed from terminal ileum	⇒ Rapidly absorbed from proximal jejunum

☆ Aetiology of Vit. B12 & folic acid deficiency:

	Causes of Vit. B12 ↓↓	Causes of Folic acid ↓↓
1- ↓ Intake:	* Very rare except breast feeders of vegetarian mothers	* Not Common. 1-Goat milk 2-Excess heated milk
2- ↓ Absorption	1-Generalized malabsorption 2-IF ↓↓→ pernicious anemia 3-IF/B12 Consumption (Diphyllobothrium latum or bacterial overgrowth) 4- Ileal disease or resection	1- Generalized malabsorption 2- ↓ folic acid absorption by drugs (Anticonvulsant drug) 3- ↓ folic acid metabolism by drugs (trimethoprim, pyrimethamine)
3- Others	<u>Defective Transport:</u> - Transcobalmin II deficiency	<u>Increase requirements:</u> - Prematurity (↓Stores) - Leukaemia and chronic hemolysis

☆ Clinical Manifestations:

- 1- General picture of anemia
- 2- GIT manifestations esp. with folic acid ↓↓ (red glazed tongue, abd. pain, colic, ...)
- 3- CNS manifestations only with severe B12 ↓↓ (Subacute combined degeneration)
 - ♦ Posterior column degeneration
 - ♦ Peripheral nerve degeneration
 - ♦ Pyramidal tract lesion

☆ Investigations:

1- For anemia ↓ RBC' s & ↓ Hb

2- For megaloblastic anemia:

- ❖ CBC : - Macrocytic anemia (↑ MCV > 95 fl & ↑ or normal MCH)
 - Reticulocytopenia , ± Leukopenia & Thrombocytopenia.
- ❖ Bone Marrow:- Megaloblastic changes
- ❖ Blood chemistry: -↑ serum LDH and iron

3- For the cause:

❖ B12 deficiency:

- i- Low serum B12 (<100 Pg/ml)
- ii- Methyl malonic acid: excess secretion in urine
- ii- Schilling test: IM large dose of non radioactive B12 (1000 µg.) to fill B12 stores, followed by oral small dose (2µg) of radioactive B12.
Normally 10-30% of the radioactive B12 will be excreted in urine.
- In case of megaloblastic anemia due to ↓B12 absorption < 2% will be excreted.
- If the excretion is ↑↑ by IF addition, IF deficiency will be the cause.

❖ Folic acid deficiency:

- i- Low serum folate (<5 ng/ml)
- ii-FIGLU Test: Excess FIGLU secretion in urine after an oral dose of histidine

☆ Differential Diagnosis:

Other causes of macrocytic anemia:

- 1- Megaloblastic anemia (B12 & folic acid ↓ / Lesch Nyhan / orotic aciduria)
- 2- B.M. failure (aplastic or hypoplastic anemias)
- 3- B.M. infiltration (leukemia, myelofibrosis).
- 4- B.M. response to hemolysis or hge.
- 5- Others (Cretinism / Down syndrome / liver disease)

☆ Treatment:**1- Treatment of the cause****2- In cases of vit. B12 deficiency:**

- ❖ If Associated with neurological manifestations 1000 µg IM daily for at least 2 weeks then maintenance therapy 1000 µg IM/month for life
- ❖ If not associated with neurological manifestation 1000 µg B12 IM/month for life.

3- In cases of folic acid deficiency:

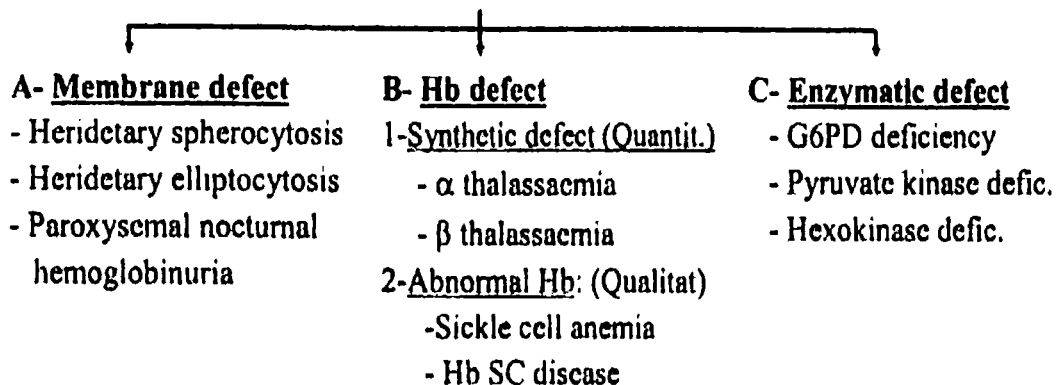
- ❖ Initially low dose of folic acid 50 µg/day is given, as large doses may worsen the neurological conditions in cases of B12 deficiency.
- ❖ If the response to ttt occurs (↑Hb% & Reticulocytosis), the full dose of folic acid is given (5 mg/day/oral) for at least one month.

D- Hemolytic Anemia

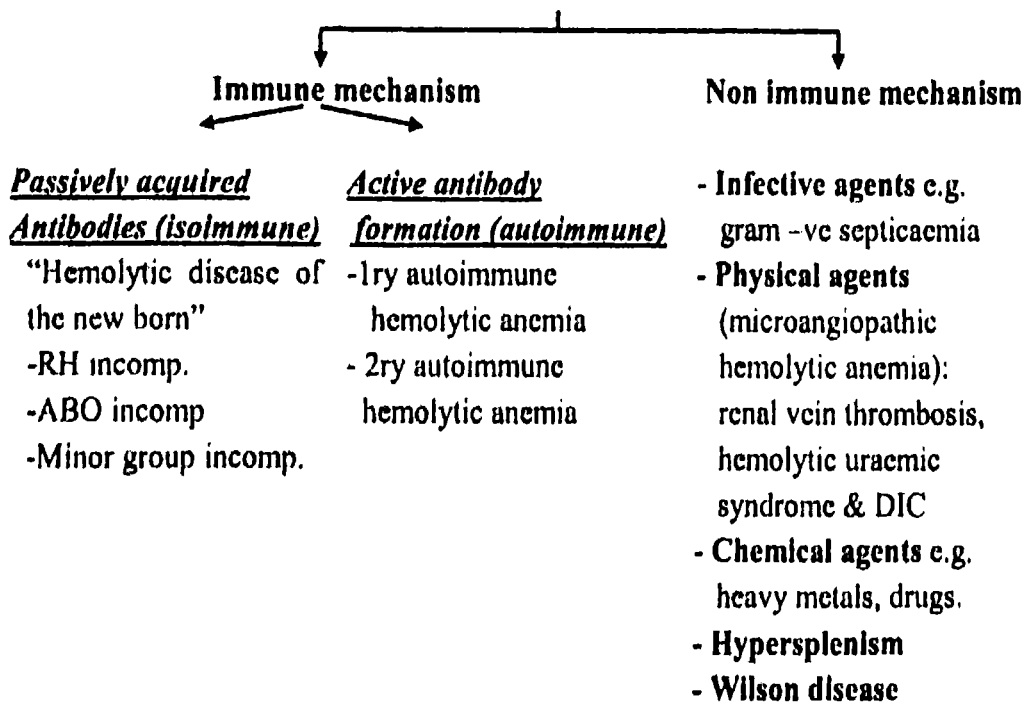
- ❖ Anemia resulting from increase destruction of RBC's
- ❖ Normal bone marrow can increase its output of RBC's production up to 7 folds during stress, so manifestations of hemolysis do not occur until severe reduction of RBC's life span occurs. Activation of the extramedullary hematopoietic tissues especially in the abdominal viscera may also occur

C Causes:

I. Intracorpuseular defects



II- Extracorpuseular defects



N.B. Hemolytic anemia can be also classified into:

1- Acute hemolytic anemia e.g. G6PD deficiency

Most of extracorporeal defects

Hemolytic crises of chronic hemolytic anemia

2- Chronic hemolytic anemia e.g. thalassaemia and sickle cell anemia.

C. Manifestations of hemolytic anemia:

1- Manifestations of anemia: See before

2- Manifestations of hemolysis:

I- Chronic hemolytic anemia

- ❖ *Tinge of jaundice*: due to excess bilirubin from Hb destruction.
- ❖ *Hepatosplenomegaly*: (due to extramedullary hematopoiesis to compensate for hemolysis and iron deposition in RES).
- ❖ *Gall stones*: pigmented gall stones develop on long-standing hemolysis (formed of calcium bilirubinate)
- ❖ *Characteristic skeletal manifestations*: hyperplasia of the erythropoietic marrow leads to expansion of the medullary spaces in the skull & hands:
 - ♦ Skull ⇒ large, prominent maxillae, protruded upper central incisors (Mongoloid face)
 - ♦ Hands ⇒ Broad & light
- ❖ *Hematological crises*:
 - ♦ Aplastic crises ⇒ Transient attacks of bone marrow failure occurs in patients with chronic hemolytic anemia especially when exposed to infection as Parvovirus B19, manifested by ↑pallor without jaundice.
 - ♦ Megaloblastic crises ⇒ folic acid deficiency on top of chronic hemolysis
 - ♦ Hemolytic crises ⇒ Precipitated by infection manifested by ↑pallor & jaundice + dark urine (hemoglobinuria).

II- Acute hemolytic anemia

- ❖ *Acute attacks of*: pallor, jaundice, dark urine (hemoglobinuria) ± fever

3- Manifestations of the cause: See later

C Investigations of hemolytic anemia:**1- Investigations for anemia:**

- ❖ Low hemoglobin
- ❖ Low RBC's count (than normal values for age, sex).

2- Investigations for hemolysis:**❖ *Indirect evidence of hemolysis:***

- 1- Reticulocytosis in peripheral blood.
- 2- Blood chemistry:
 - ♦ ↑ unconjugated bilirubin & serum iron
 - ♦ ↓ plasma haptoglobin & hemopexin
- 3- Radiological signs (**in chronic hemolysis**):
 - ♦ Gall stones can be detected by X-ray or ultrasound
 - ♦ Skull X-ray shows: macrocephaly, widening of the diploic space with hair on end appearance.
 - ♦ Hand X-ray shows rarefaction (↓ density) and barrel shaped metacarpals.

❖ *Direct evidence of hemolysis:*

- Presence of hemoglobin in urine (hemoglobinuria) → in acute hemolysis
- Estimation of RBC's survival by isotope techniques e.g. sodium chromate.

- 3- **Bone marrow**: shows erythroid hyperplasia, may be aplastic in aplastic crisis or megaloblastic with ↓ folic acid.

HEREDITARY SPHEROCYTOSIS

C Aetiology:

Autosomal dominant disease characterized by abnormal RBC's membrane.

C Pathogenesis:

- * Abnormality in cell membrane lipoprotein (spectrin) → ↑Na⁺ permeability into the cell → ↑ATPase activity & glucose consumption at the membrane to get the excess Na⁺ outside the RBC's → Premature aging of RBC's
- * ↑ Na⁺ influx → ↑water content inside the cells → swelling of RBC's which becomes early destructed especially in sinusoids of the spleen 

C Clinical manifestations:

- * As any case of chronic hemolytic anemia with:
 - 1- Onset may be during neonatal period leading to neonatal anemia & jaundice.
 - 2- Pigmented gall stones are commoner than other causes of hemolytic anemia especially during late childhood.
 - 3- splenomegaly

C Investigations:

- * As any case of chronic hemolytic anemia .

- * Investigations for spherocytosis:

- 1- Peripheral blood → spherocytes (small rounded RBC's with loss of its central pallor)
- 2- Osmotic fragility test →

Idea: When RBC's are placed in hypotonic solution they imbibe water and become swollen. As hypotonicity of the solution increased the rate of water flow inside the RBC's ↑↑till rupture of RBC's occurs.

Normally: The rupture: * Begins at 1/2 tonic solution (0.45% saline)
 * Completed at 1/3 tonic solution (0.3% saline)

In spherocytosis: The cells are already swollen so osmotic fragility is increased.

The rupture: * Begins at 3/4 tonic solution (0.75% saline)
 * Completed at 1/2 tonic solution (0.45% saline)

- 3- Auto hemolysis test →

If RBC's are incubated for 2 days at 37 C° →

- Normally → <5% of RBC's are hemolysed.
- In spherocytosis → 15-30% of RBC's are hemolysed (as spherocytes are deficient in glucose support, so → if glucose is added → ↓hemolysis)

C Treatment:

- 1- Blood or RBC's transfusion if anemia is severe and during crises.
- 2- Splenectomy: Cure the patients by preventing hemolysis & crises but not correct the morphology of RBC's.

Precautions: 1- Not done before 5 years old to prevent salmonella osteomyelitis H.influenza and meningococcal or pneumococcal infections.

2- Vaccination against pneumococci & H.influenza before operation.

3- Prophylactic penicillin after operation till adult life.

GLUCOSE 6 PHOSPHATE DEHYDROGENASE DEFICIENCY "favism"

C Aetiology:

XR disorder (male > female) due to deficiency of G6PD enzyme in RBC's

C Pathogenesis:

- * **G6PD is the enzyme** necessary in HMP shunt which result in formation of reduced glutathion that protects the RBC's against oxidizing agents.
- * **In G6PD deficiency**, Glutathion is oxidized → exposure to oxidizing agent lead to precipitation of hemoglobin on the inner side of RBC's membrane (Heinz bodies) and their destruction.
- * **Oxidizing agents include:**
 - 1- Food: especially fava beans.
 - 2- Infections: pyogenic infections.
 - 3- Drugs: Antimalarial → Quinine & quinidine
 Antipyretics → Salicylates.
 Antituberculous → INH & paraaminosalicylic acid
 Antimicrobials → Sulpha & Chloramphenicol

C Clinical manifestations:

Manifestations of hemolysis as before develop in 3 forms:

- 1- **Acute hemolysis** → Rapid deterioration occurs 12-24 hours after ingestion or contact with the oxidizing agent in the form of acute pallor, jaundice & dark urine ± fever.
- 2- **Neonatal anemia & jaundice**
- 3- **Chronic hemolysis** → Rare

C Investigations:

- * General investigations for hemolysis
- * During the attack Heinz bodies appear in RBC's (Blood film)
- * 1-2 months after the attack enzymatic assay of G6PD reveals low amount of the enzyme in blood (not measured during the acute attack as RBC's with low enzyme level will be destructed).

C Treatment:

⇒ Prophylactic:

- 1- Identification of the patients who are given cards referred to their disease (G6PD ↓ patients)
- 2- Avoid foods & drugs which predispose to hemolysis in known G6PD ↓ patients.
- 3- In febrile child with G6PD ↓ paracetamol is given (safe)

⇒ Curative: (during the attack)

- 1- Stop intake of any oxidizing agent.
- 2- Packed RBC's transfusion (5-10ml/kg) & may be repeated in severe hemolysis

C Prognosis:

- ✦ The disease tends to improve with age.
- ✦ Spontaneous recovery from hemolytic crises is the normal outcome

THALASSAEMIAS

AR disorders characterized by defective globin synthesis ($\downarrow$ production of one globin chain)

❖ Defective α chain production $\rightarrow$ α thalassaemia (4 genes are responsible for α chain formation) so, if:

- $\rightarrow$ 4 genes affected $\rightarrow$ Still birth
- $\rightarrow$ 3 genes affected $\rightarrow$ HbH disease (severe)
- $\rightarrow$ 2 genes affected $\rightarrow$ α thalassaemia trait (Mild)
- $\rightarrow$ 1 gene affected $\rightarrow$ Silent carrier

❖ Defective β chain production $\rightarrow$ β thalassaemia (2 genes are responsible for β chain formation so if:

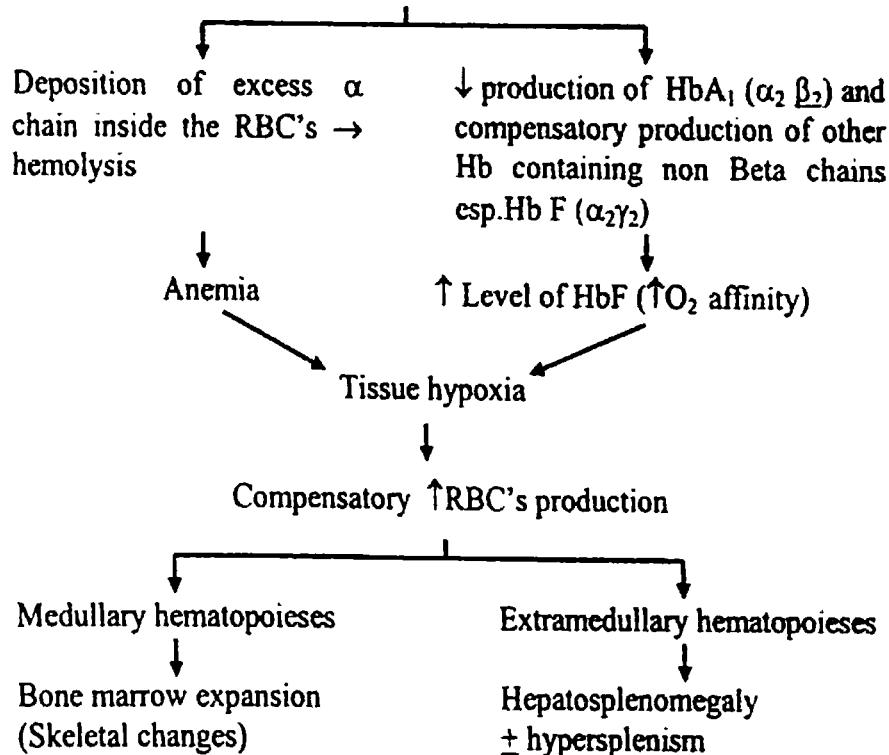
- $\rightarrow$ 2 genes affected $\rightarrow$ β Thalassaemia Major.
- $\rightarrow$ 1 gene affected $\rightarrow$ β Thalassaemia. Minor

β -Thalassaemia major: (Cooley's anemia)

The most common cause of ch. hemolytic anemia in Egypt & Mediterranean areas.

C. Pathogenesis:

1- $\downarrow\downarrow\downarrow$ β chain production Leading to



2- Iron $\uparrow\uparrow$ secondary to:

- ❖ Compensatory $\uparrow$ intestinal absorption of iron.
- ❖ Repeated blood transfusion.
- ❖ Hemolysis of RBC's

* ($\uparrow$ serum iron $\rightarrow$ Deposition of iron in various organs = hemosiderosis)

C C/P:

- 1- **Manifestations of anemia** (see before)
- 2- **Manifestations of chronic hemolytic anemia including crises.** (see before)
- 3- **Specific features of thalassaemia:**
 - ❖ Age must be above 6 months old (when β chain becomes predominant).
 - ❖ Mongoloid features & HSM are typical esp. long standing cases
 - ❖ Hemosidrin (iron deposition)
 - ♦ Skin → Bronzed colour
 - ♦ Liver & spleen → HSM
 - ♦ Pancrease → DM
 - ♦ Heart → Cardiamyopathy
 - ♦ Pituitary → Hypopituitarism(with GH ↓ and short stature).

C Investigations:

- 1- **Investigations for anemia.**
- 2- **Investigations for hemolysis.**
- 3- **Specific investigations for β -Thalassaemia major:**
 - ❖ Blood film: - Microcytic hypochromic anemia
- Target cells (centrally nucleated Hb) 
 - ❖ Hb electrophoresis: ↓ HbA & ↑ HbF (all cases) & ↑ HbA₂
 - ❖ Genetic counseling: Premarital for high risk families
 - ❖ Prenatal diagnosis programs by chorionic villous sampling (CVS).
- 4- **Investigations for iron overload:**
 - ❖ Iron studies : serum iron , ferritin , transferrin saturation and TIBC.
 - ❖ Magnetic resonance imaging: Assess iron loading in the liver, heart, and, pancreas.
 - ❖ T2*: Magnetic resonance for the early diagnosis of myocardial iron overload.
 - ❖ Superconducting quantum interface device (SQUID) Noninvasive quantitate of hepatic iron stores.

C Complications & causes of death:**1- Frequent blood transfusion:**

- Febrile reaction
- Allergic reaction
- Disease transmission (Hepatitis, AIDS, syphilis,.....)
- Incompatible blood transfusion

2-Failure of the heart:

Anaemic heart failure if no blood transfusion is given, while excess transfusion may ↑ load on the heart due to hypervolaemia.

3- Growth retardation and delayed puberty and endocrinopathies.

4- Hypersplenism: with resultant pancytopenia.

5- Hemosiderosis: see before

6- ↑Susceptibility to infection.

C Management:

1- Regular packed RBC's transfusion:

- * 10-15 ml/kg every 4-6 weeks is sufficient to keep Hb level above 10gm/dl. Frequent transfusion will keep Hb level above 12 gm/dl (super transfusion).
- * Regular blood transfusion will permit normal growth, ↓ organomegaly and minimize skeletal changes

2- Iron chelating agents:

- * Deferoxamine (Desferal): 25-50 mg/kg/day IM, I.V. or better continuous S. C. pump for 12 hours/day → 5-7 days/week
- * Oral chelating agents:
 - a- Deferiprone (L1): more compliance for the patients, absorption is rapid from the stomach, the dose is 50-75mg/Kg. Gastrointestinal troubles and agranulocytosis are risky complications.
 - b- Exjade (ICL 670): more compliance for patients, taken once daily at the morning, the dose: 30-40 mg/kg.

3- Dietary support:

- * Good caloric intake with suitable ratios of food elements.
- * Folic acid supply (1mg/day) oral to prevent megaloblastic crises, as folic acid deficiency is common in β -thalassaemia due to hyperactive bone marrow with depletion of folate stores in new RBC's synthesis.
- * Iron is contraindicated.

4- Treatment of crises:

- * Packed RBCs transfusion ± treatment of infection.

5- Splenectomy:

* *Indicated in*

- ♦ huge spleen causing severe pressure symptoms
- ♦ hypersplenism → indicated by increase the amount of transfusion than usual (> 250 ml / kg / year) or appearance of pancytopenia.

* *Precautions:*

See spherocytosis

*** Recent treatment of thalassemia:**

- 1- Young RBCs (neocytes) transfusion to increase life span of the RBCs.
- 2- Bone marrow transplantation.
- 3- Population screening and prevention.
- 4- Gene therapy: Introduction of new genetic information into marrow cells results in activation of the γ globin genes and decreased amount of unbound α chain (fetal Hb augmentation). Hydroxyurea also augments Hb F.

C Prognosis:

Most of the patients die from complications between 20-30 yrs old

β -Thalassaemia minor: → Heterozygous form:

- Most of the patients have no or very mild symptoms. Accidental appearance of microcytic anemia in CBC is the usual finding and it must be D. D. from Iron deficiency anemia.
- Diagnosis: * $\uparrow$ HbF (only present in 50% of cases) * $\uparrow$ Hb A₂ (diagnostic)

Hereditary persistence of foetal Hb: HPFH

A condition associated with presence of HbF instead of HbA which is normally distributed in RBC's with no excess α chine so very mild anemia is present + Good prognosis.

SICKLE CELL HEMOGLOBINOPATHY

- Autosomal recessive disorder characterized by qualitative defect in globin synthesis in which substitution of amino acid number 6 (glutamic acid) in β -chain by valine occurs, leading to formation of abnormal hemoglobin (HbS) → which can't withstand hypoxia

□ Pathogenesis:

- * Exposure to hypoxia → Hb distortion and abnormal shape of RBC's (Sickling)
- * These abnormal cells aggregate, leading to vascular obstruction and early destructed (hemolysed RBCs) by the R. E. S.
- * 2 forms are present:
 - Homozygous form → sickle cell anemia
 - Heterozygous form → sickle cell trait

Sickle cell anemia: → Homozygous form (SS)

□ Clinical manifestations:

- ✧ Manifestations of anemia. "see before"
- ✧ Manifestations of chronic hemolysis. "see before"
- ✧ Specific manifestations of sickle cell anemia:
 - 1- Presentation after 6 months old
Common in Negroes.
 - 2- Leg ulcers are common.
 - 3- Renal impairment is common (even nephritis & haematuria).
 - 4- Splenomegaly initially is followed by shrinkage as a result of repeated splenic infarctions (autosplenectomy) This defective spleen may be associated with infections (see hyposplenism).
 - 5- The same crises as usual, but other crises may occur in sickle cell anemia:
- ✧ Vaso-occlusive crises: The most frequent, precipitated by hypoxia (anaesthesia, pneumonia, shock, dehydration, acidosis,)
 - ✧ Hand foot syndrome → infarction in small bones of extremities (symmetrical bone pain & swellings)
 - ✧ Pulmonary infarction → chest pain, hemoptysis (sickle chest syndrome).
 - ✧ Stroke → Due to cerebral artery occlusion.
 - ✧ Hematuria → Due to renal infarction.
 - ✧ Autosplenectomy.
- ✧ Sequestration crises: precipitated by dehydration; occurs in patients < 2 years. Sudden pooling of the blood in the spleen → shock, massive splenomegaly.
- ✧ Hyperhemolytic crises: Due to associated G6PD↓.

❑ Investigations:

1- Investigations for anemia.

2- Investigations for hemolysis

3- Special investigations for sickle cell anemia:

- * Sickle cell in peripheral blood, if not detected sickling can be enhanced by adding Na metabisulfite.)))
- * Hb electrophoresis → shows HbS (90%) and HbF (2-10%)
- * Prenatal diagnosis by chorionic villous sampling & DNA analysis.

❑ Treatment:

⊕ The same lines for thalassaemia except splenectomy:

⊕ Treatment of crises:

- ⊕ Analgesics & good hydration for vaso- occlusive
- ⊕ Blood transfusion for hemolytic & aplastic crises
- ⊕ Antishock measures, blood & even emergency splenectomy are indicated in sequestration crises

⊕ Treatment of autosplenectomy: (Vaccination + penicillin → see spherocytosis)

Sickle cell trait: → heterozygous form (AS)

- ♦ The patient's blood contains mixture of (HBS) and (HBA)
- ♦ Normally asymptomatic but severe hypoxia may lead to crises
- ♦ Patients are resistant to falciparum malaria.

AUTOIMMUNE HEMOLYTIC ANEMIA

□ Definition:

"Hemolytic anemia due to circulating antibodies against patient own RBCs"

Two theories are present to explain the production of the abnormal antibodies against RBCs.

- 1- Altered immune response (loss of self tolerance).
- 2- Altered RBCs antigenicity by infection or drugs.

* According to the type of antibodies produced, AIHA are classified into two categories.

A- Auto - Immune Hemolytic Anemia due to Warm Antibodies:

* Antibodies are of IgG class, active at 37°C, do not need complement for activity.

*** Causes:**

- (1) 1ry or idiopathic .
- (2) 2ry or symptomatic, associated with:
 - 1- Auto - immune diseases as SLE.
 - 2- Viral infections e.g. EBV , HBV .
 - 3- Lymphoma or other malignancies.
 - 4- Drugs: Penicillin, methyl dopa, cephalosporins, phenacetin.

*** Mechanism:**

The warm Abs coat the RBCs lead to cell membrane injury and microspherocytosis.

*** Clinical picture:**

Two clinical features are present : Acute and chronic

<i>Acute transient type</i>	<i>Chronic type</i>
- age: 2-12 year.	- age: < 2 or > 12 years
- usually follow respiratory infection.	- underlying systemic disease e.g. lymphoma.
- acute hemolytic anemia and splenomegaly	- chronic hemolytic anemia
- good response to steroids	- variable response to steroids.

B- Auto - immune Hemolytic anemias due to cold antibodies.

Antibodies against RBCs are of IgM class, more active at low body temperature (cold antibodies) and require complement for their activity.

Two clinical types are recognized, which are

1- Cold agglutinin Diseases:

It is either: *primary* (idiopathic), or *secondary* to infections as EB virus, mycoplasma pneumoniae or lymphoreticular malignancies.

2- Paroxysmal Cold Hemoglobinuria:

- Due to specific antibody "Donath- Landsteiner antibody".
- 1/3 of cases are 2ry to syphilis; congenital or acquired.

B) For Acute Hemolysis: decreased RBCs survival and increased erythropoiesis.

1- Blood film; microspherocytes.

3- If associated with auto-immune thrombocytopenia, the condition is called "Evan's syndrome".

1- Treatment of the cause: in 2ry causes & avoidance of cold

3- Washed packed RBCs transfusion to correct anemia. It is very difficult to find a compatible blood by cross- matching.

5- Immunosuppressive drugs are used in resistant cases.

7- Recently : I.V Gamma globulin infusion.

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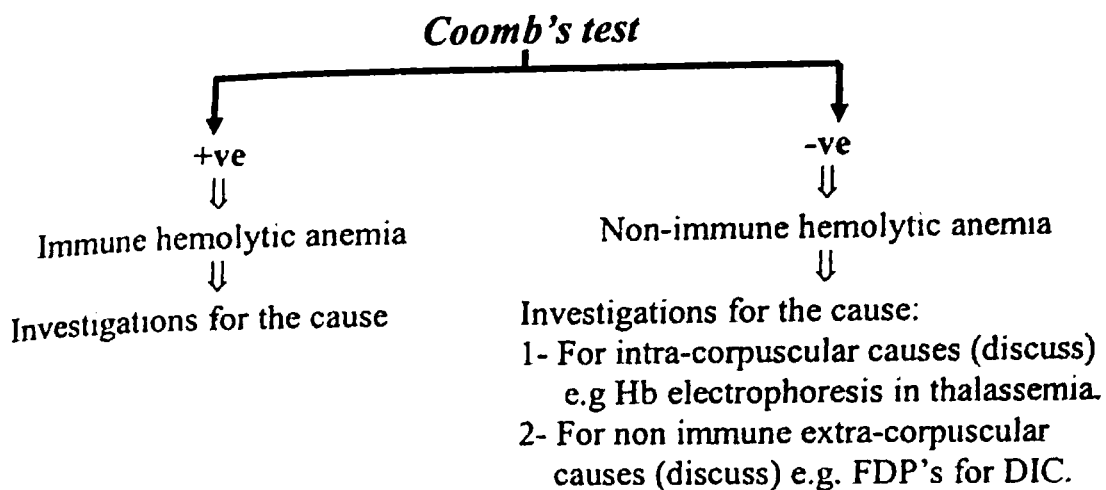
HOW TO INVESTIGATE A CASE OF ANEMIA

1- Diagnosis of anemia:

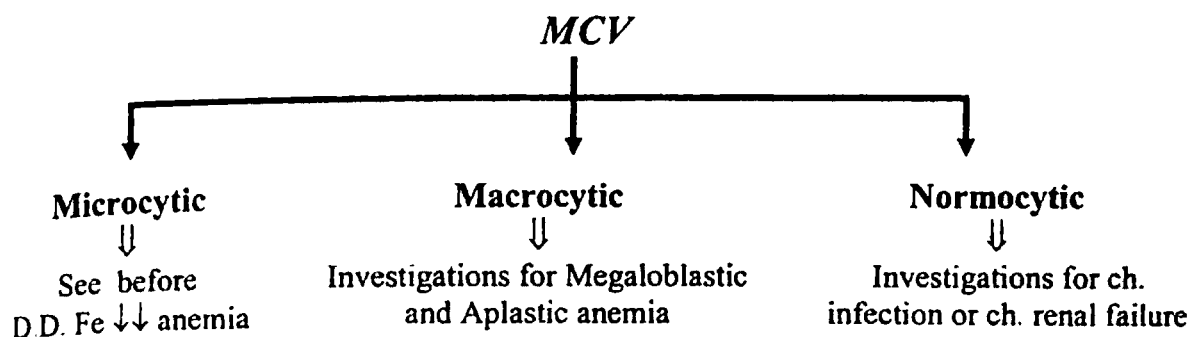
- ↓ Hb %.
 - ↓ RBC's count
- ⇒ in CBC

2- Full history and examination to exclude anemia due to blood loss (Hemorrhagic anemia)

3- Perform investigations for hemolysis (discuss) esp. Reticulocytic count. if these tests are +ve it's a case of (Hemolytic anemia).



4- If the hemolytic investigations (esp. Reticulocytic count) are -ve, It will be (Anemia due to ↓ production)



CAUSES OF SPLENOMEGALY

In	Hematology	Malignancy	May	Cause	Chronic	Congestion
↓	↓	↓	↓	↓	↓	↓
Infection	Hematological	Malignancy	Metabolic	Collagen	Cysts	Congestion

1- Infection:

	Acute infection	Chronic infection
▪ Bacterial	⇒ Typhoid, SBE, sepsis	⇒ Miliary T B. & Brucellosis
▪ Viral	⇒ CMV, EBV	⇒ Congenital infections (TORCH)
▪ Protozoal	⇒ Malaria, kala-azar	⇒ β
▪ Spirochetal	⇒ Leptospirosis	⇒ S

2- Haematological:

* Haemolytic anemia * Polycythaemia * Iron ↓ anemia (10%) * Hypersplenism.

3- Malignancy:

* Leukaemia * Lymphoma * Neuroblastoma

4- Metabolic:

* Amino acid, Fat & CHO storage diseases.

5- Collagen:

* SLE * Rheumatoid arthritis * Sarcoidosis * Amyloidosis

6- Cysts of the spleen**7- Congestive splenomegaly: = All causes of portal hypertension**

☞ **N.B. Huge spleen** (Spleen which cross the mid line)

- Gaucher, sarcoidosis, amyloidosis
- CML & polycythaemia & Thalassemia major
- β & Malaria & Kala-azar

HYPERSPLENISM

* Splenomegaly due to any cause may be associated with hypersplenism

(↑ splenic function) leads to ↑↑ destruction of RBC's, WBC's & platelets.

* **C/P:** Bleeding (↓ plat) / infection (↓ WBC's) / hemolytic anemia (↓ RBC's).

* **Invest:** • Blood → ↓ WBC's & platelets + Hemolytic anemia !! (discuss).

• BM → normal or hypercellular

* **TTT:** • Mild → no ttt

• Severe → surgical splenectomy or splenic embolization

HYPOSPLENISM

- * Defective or absent splenic function which occurs in → congenital asplenia, post-splenectomy or autosplenectomy in sickle cell anemia
- * **C/P:** ↑ risk of sepsis (pneumococcal infec./H.influenza & salmonella osteomyelitis)
- * **Invest:**
 - Blood → Howel-Jolly bodies.
 - TC isotop scan → absent splenic tissues.
- * **TTT:**
 - Vaccination against pneumococci & H.influenza.
 - Prophylactic penicillin till adult life.
 - If splenectomy is not urgent it is better delayed after the age of 5 years

HEMORRHAGIC DISORDERS

- Hemostasis is the mechanism of stoppage of bleeding after injury of a blood vessel. Different factors are encountered in this process, which are:

1- Vascular factors:

❑ Vascular role in hemostasis:

- Reflex vasoconstriction at the site of bleeding
- Damaged vascular endothelium activates factor 12 which initiates the intrinsic pathway of clot formation
- Exposed collagen fibers is the site of platelet aggregation

❑ Investigations for vascular integrity:

- 1- Bleeding time: (Normally 3-5 min.)
- 2- Capillary fragility test: (Hess test): the blood pressure cuff is inflated between systole and diastole for 5 minutes. If more than 5 petichae appears within 2.5 cm diameter in the forearm the test is considered +ve

❑ Vascular abnormalities:

I- Inherited:

- ❖ Ehler Danlos syndrome: (AD) with hyperelasticity of skin & joints.
- ❖ Marfan syndrome: (AD) with tall stature and dislocated lens.
- ❖ Ataxia telangiectasia: (AR) with associated ataxia.

II- Acquired:

- ❖ Henoch-Schonlein purpura: (The most common)
- ❖ Sepsis: Especially meningococcal septicaemia & SBE
- ❖ Scurvy (vit. c deficiency).
- ❖ Steroid excess (Cushing syndrome)

2- Platelets:

❑ Functions of platelets:

- 1- Platelet adhesion: to the exposed collagen fibers (Von Willebrand factor is essential for this process).
- 2- Platelet aggregation: Platelet clumps to each other, this process is helped by ADP & thromboxane A₂.
- 3- Release:
 - ADP & thromboxane A₂ (↑ aggregation)
 - Serotonine (vasconstriction of vessels)
 - Platelet factor 3 (enhances clotting)
 - Thrombasthenin (for clot retraction)
- 4- Platelet plug formation: By fibrin deposition within it

□ **Investigations for platelet assessment:**

- 1- Bleeding time
- 2- Capillary fragility test (Hess test)
- 3- Platelet count (Normally 150,000-400,000/C.C)
- 4- Platelet function test:
 - ♦ Clot retraction test
 - ♦ Aggregometer to assess aggregation.
 - ♦ Quantitation of PF3 level

2- Platelet Abnormalities:

I- Qualitative (Thrombasthenia):

□ **Inherited:**

- ✦ Defective adhesion: Von Willebrand disease & Bernard Soulier disease
- ✦ Defective aggregation: Glanzman disease.
- ✦ Defective secretion: Storage pool disease.

□ **Acquired:**

- ✦ Drug induced thrombocytopathy (Salicylates & NSAID's)
- ✦ Uraemic induced thrombocytopathy (in chronic renal failure)
- ✦ Systemic disease induced thrombocytopathy (leukaemia, cirrhosis, ...)

II- Quantitative (thrombocytopenia):

□ **Inherited:**

① **↓ Production:**

- Fanconi anemia.
- Thrombocytopenia absent radius syndrome (TAR).
- Wiskott Aldrich syndrome (eczema and immunodeficiency).

② **↑ Destruction:**

- Thrombocytopenia with cavernous hemangioma (Kasabach-Meritt S.).
- Giant platelet disorder (May – Hegglin anomaly).

□ **Acquired:**

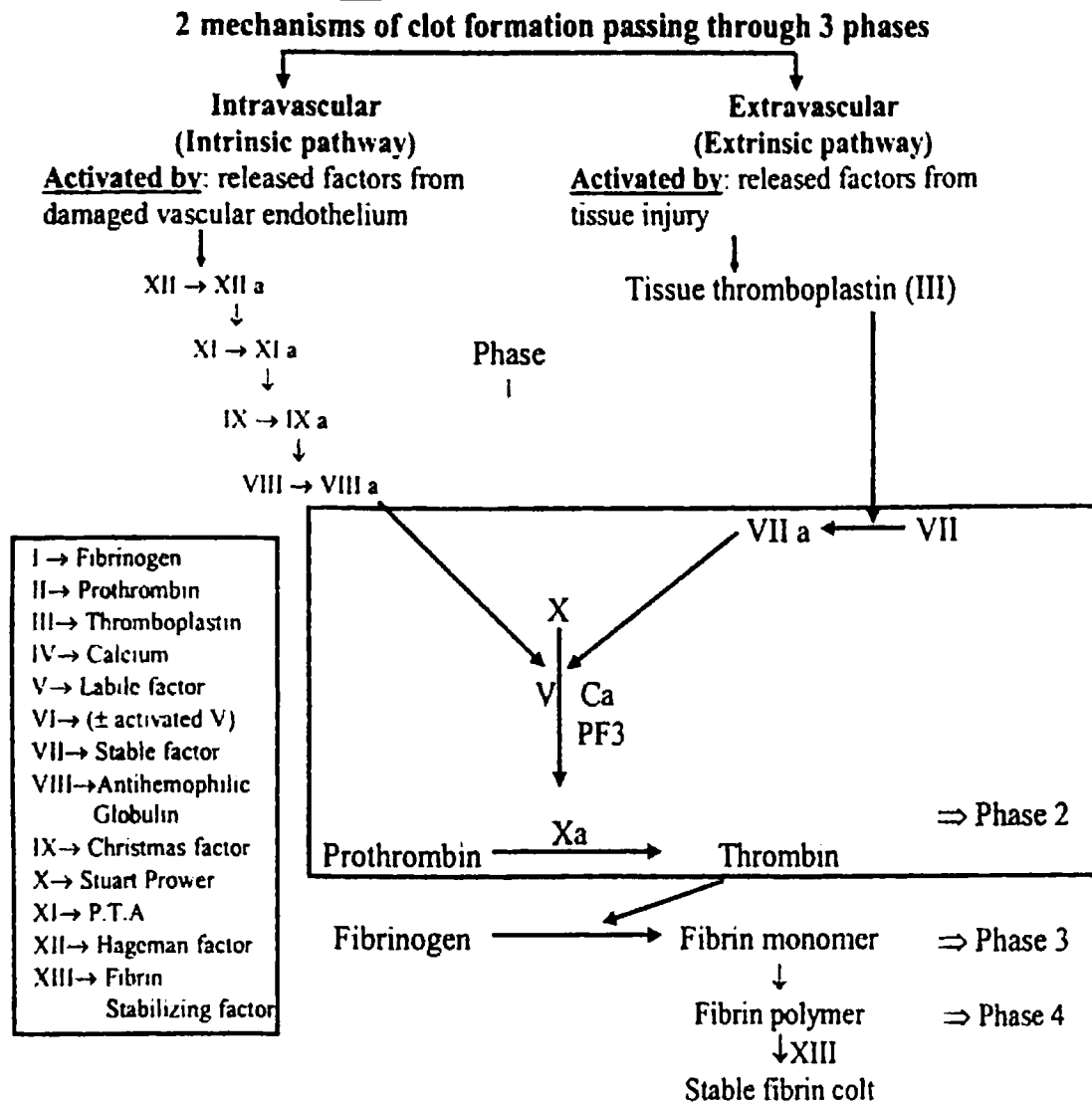
① **↓ Production:**

- Aplastic anaemia
- Megaloblastic anemia
- B.M. infiltration.

② **↑ Destruction:**

- Idiopathic thrombocytopenic purpura (ITP) → the commonest.
- SLE
- Infection e.g. Rubella, I.M.N.
- Hypersplenism.
- DIC.

3- Coagulation factors



□ Assessment of coagulation factors:

1- Assessment of phase IV:

Defective formation of firm fibrin network (e. g. F XIII ↓) can be assessed by solubility of the blood clot when placed in a solution of monochloroacetic acid.

2- Assessment of phase III:

- ✧ Thrombin time (N. 15-20 sec.) which may be prolonged if factor I is deficient.
- ✧ Quantitation of factor I (Fibrinogen level) is available

3- Assessment of phase II:

- ✧ Prothrombin time (N. 12-14 seconds) which may be prolonged in deficiency of any of factors II, V, VII, X
- ✧ Quantitation of these factors separately is available.

4- Assessment of phase I:

- ✧ Partial thromboplastin time (N. 25-40 seconds) which may be prolonged in ↓↓ of any of factors VIII, IX, XI, XII ⇒ Also thromboplastin generation test is helpful.
- ✧ Quantitation of these factors separately is available.

5- The whole coagulation process:

Can be roughly evaluated using the clotting time (N. 7-12 min.) which if prolonged may suggest a problem in any phase of coagulation.

□ Coagulation abnormalities:

* Phase (I) disorders:

- i- Factor VIII deficiency (Hemophilia A-classic hemophilia) → XR.
- ii- Factor IX deficiency (Hemophilia B-Christmas disease) → XR.
- iii- Factor XI deficiency (Hemophilia C) → AR (rarely AD).
= mild bleeding and epistaxis
- iv- Factor XII deficiency (Hageman disease) → AR (rarely AD).
- v- Von Willebrand disease (Vascular hemophilia) → AD.

* Phase (II) disorders:

- i- Congenital absence of factor V or VII.
 - ii- Acquired disorders:
 - Liver disease - Vit. K deficiency - Hgic disease of the newborn.
- N.B. Vit. K is essential for factor II, VII, IX & X synthesis.

* Phase (III) disorders:

- i- Congenital afibrinogenemia (AR) = ↓↓ fibrinogen level.
- ii- Congenital dysfibrinogenemia (AD) = ↓↓ fibrinogen action.

* Phase (IV) disorders:

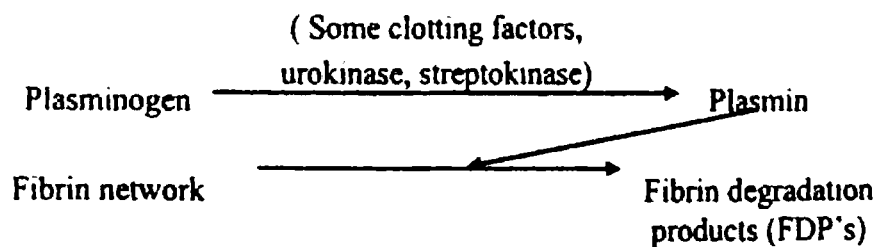
- Congenital factor XIII deficiency (AR).

* Multiple phases defect:

- DIC may result in consumption of multiple coagulation factors especially factor II, V, VIII.

4- Fibrinolytic system:

- ÷ If the process of coagulation continued it will lead to occlusion of blood vessels and disseminated thrombosis
- ÷ So, at the beginning of coagulation process activation of another system (The fibrinolytic system) occurs which dissolve the thrombus and recanalize blood vessels after the end of coagulation process



□ Evaluation of the fibrinolytic activity: FDP's is increased in cases of DIC.

□ Fibrinolytic defects:

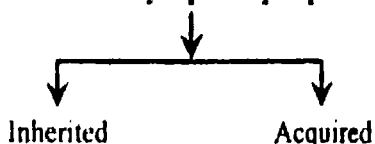
- * ↑ Plasmin level → ↑ fibrinolysis → Hge.
- * DIC (consumption coagulopathy).

A- PURPURA

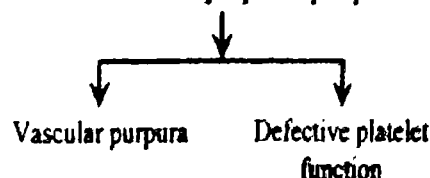
- ❑ **Definition:** Multiple spontaneous hemorrhages in the skin and mucous membranes producing areas of purple discolouration, they range from pin-point (petechiae) to large sized (ecchymosis).
The purpuric eruptions do not blanch on pressure
- **N.B.:** Purpura (vascular or platelet defect / mainly petechiae / spontaneous bleeding)
Hemophilia (coagulation defect / mainly ecchymosis / induced bleeding)

❑ Causes:

Thrombocytopenic purpura



Non thrombocytopenic purpura



❑ Approach to a case of purpura:

I- Is it Purpura or not?

DD from other causes of maculopapular rash esp. flea bite.

II- It is Purpura. What is the cause?

⊕ History:

- Preceding URTI may suggest ITP or HSP.
- Prolonged fever may suggest leukemia.
- Convulsions may suggest meningococcaemia.
- Dietetic history for scurvy.
- Drug history for steroid intake.
- Family history for genetic problems e.g. Marfan, Ehler Danlos, Ataxia telangiectasia, ...

⊕ Exam:

- HSM → Leukaemia.
- Cushingoid face → Steroid excess.
- Pallor without HSM → Aplastic anemia.
- Arthritis + renal → HSP.
- Tall stature → Marfan.
- Poor wound healing → Scurvy.
- Eczema → Wiskott Aldrich.
- Normal exam → ITP.

⊕ Investigations:

* Bleeding profile:

- Bleeding time.
- Hess test.
- Platelet count
- Platelet function
- Normal tests of coagulation.

* For the cause:

- e.g.
 - ANA for SLE.
 - BM for leukemia.
 - CBC for aplastic anemia
 - Urine for HSP.
 - X-ray radius for Fanconi & TAR.
 - Blood culture for sepsis.

Idiopathic Thrombocytopenic Purpura (ITP)

❑ **Def.**

Acquired thrombocytopenic purpura of children and adults characterized by decrease platelet count in the absence of other clinically apparent cause.

❑ **Aetiology:**

- Immune mechanism is the most postulated aetiology (so named Immune Thrombocytopenic Purpura).
- The condition usually occurs 1-4 weeks after respiratory viral infection which most probably trigger the formation of autoantibodies against platelets. Antibodies that are reactive with major membrane glycoprotein can be identified in 50-80% of patients. Most antibodies directed against glycoprotein IIb - III a.

❑ **Clinical picture:**

- 1- **Spontaneous bleeding** (but may follow mild trauma) in:
 - * The skin (petechiae, rarely ecchymosis).
 - * Mucous membrane bleeding (epistaxis, bleeding gums).
 - * Internal bleeding (Intracranial in severe cases, may be fatal 1%).
- 2- **No L.N. ++ or HSM** (10% have only palpable spleen).
- 3- **Most commonly acute type** in young children with spontaneous resolution within 2-6 weeks but chronic type may present in older children or adults characterized by intermittent remission and exacerbation lasts more than 6 months, commonly associated with splenomegaly.

❑ **Investigations:**

- 1- **Defective platelet tests:**
 - +ve Hess test • ↓↓ platelet count < 40,000 • Prolonged bleeding time.
- 2- **Bone marrow exam:**
 - Normal or ↑ megakaryocytes with defective budding.
 - Done mainly to exclude leukaemia and aplastic anemia.

❑ **D.D.:** Other causes of thrombocytopenic purpura.

❑ **Treatment:**

General measures:

Avoid trauma & salicylates and IM injections.

- Indications of medical treatment:

- 1- Platelets <20,000 with significant bleeding.
- 2- Platelets <10,000 and minor purpura.

Standard First line treatment:

Conventional Steroid therapy: 2mg/kg/day prednisone (maximum 60mg/day), given in divided doses, then reduced at 5-7day intervals, irrespective of platelet count to be stopped at 3-4 weeks.

Pulse therapy: In severe cases, methyl prednisone (Solu-Medrol) 30mg/kg/day (maximum 1g/day) for 3 days produces a more rapid response than steroids in conventional doses.

Alternate First line treatment:**1. IV Gammaglobulin (IVIG)**

Doses Of : * 0.4 g/kg/day for 5days or 1g/kg/day for 2days.

* 0.8g/kg/day as a single dose or 250 mg/kg/day for 2 days have been used with success.

These IVIG block Fc receptors of macrophages so decrease platelet destruction.

2. Anti -D Therapy

produces mild hemolysis (distract immune system).

- Precautions:

a-The patient must be **Rh positive** for this mode of therapy to beneficial

b- HB > 10 g/dl.

Second line therapy:**- Splenectomy:**

Splenectomy for acute ITP is considered as an emergency treatment in patient with life threatening hemorrhage especially intracranial who does not respond to the aggressive therapy with platelet transfusion, IVIG and IV corticosteroids.

Therapy for refractory ITP:

Other immunomodulatory therapy for patients with acute ITP non-responding to the previous standard regimen includes the following agents: cyclophosphamide , vincristine, azathioprine, colchicine and interferone .

Recent lines:

-Rituximab : anti-CD 20 .

- Eltrombopag , Romiplostim : thrombopoietin receptor agonist.

*** Intracranial Hemorrhage in ITP**

Incidence: <1%

Platelet count:

< 10,000 in 73% of cases.

10-20,000 in 25 % of cases.

>20,000 in 2% of cases.

Prognosis: can have 30 -50% mortality, but most survivors without permanent damage.

*** Management of life threatening hemorrhage including intracranial haemorrhage:**

1- Platelet transfusion.

2- Solu-medrol 500mg/ m² IV/day for 3 days.

3- IVGG 2g /kg.

4- Emergency splenectomy.

□ Prognosis:

Spontaneous recovery occurs in 80% of cases within 6 months and the remaining cases give response to steroids.

Henoch Schonlein (anaphylactoid) Purpura

- **Incidence:**
 - The most common vasculitis syndrome esp. male (2-8 yrs).
- **Aetiology:** Unknown, $\pm$ allergy, drug sensitivity, vaccination or certain infections.
- **Pathology:**
 - Most common sites: Skin, synovium, GIT, renal glomeruli and CNS.
 - Capillaries are usually involved but small arterioles may be also affected.
- **Clinical manifestations:**
 - 1- **Skin lesions:** All patients
 - * **Skin rash:** Any part but usually buttocks and lower extremities in the form of raised violet rash initially blanch on pressure then becomes purpuric, rash is rarely pruritic.
 - * **Angioedema:** lids, lips, dorsum of hands & feet and perineum.
 - 2- **Arthritis:** 2/3 of affected children:
 - Large joints (esp. LL) → swelling, hotness, redness, limitation of movements, tenderness $\pm$ effusion. Resolves spontaneously in few days without residue.
 - 3- **GIT symptoms:** > 1/2 of affected children:
 - Abd. pain is the most common
 - GIT bleeding (gross or occult blood in stool $\pm$ hematemesis).
 - Rarely intussusception, obstruction or perforation of the bowel.
 - 4- **Renal involvement:** 1/4 – 1/2 of affected children:
 - Onset during acute phase but may be weeks later..
 - Hematuria, oliguria, proteinuria and hypertension.
 - Rarely nephrotic syndrome or frank nephritis.
 - 5- **Rare manifestations:**
 - CNS: Seizures, paresis and coma.
 - Testicular: Swelling and hge.
- **Laboratory findings:** Not diagnostic → Diagnosis is mainly clinical.
 - **Coagulation profile, bleeding time and platelet count:** Normal.
 - **Serum IgA:** Elevated in 50% of the patients, with **IgA deposits** in skin biopsy.
 - **Stool:** Gross or occult blood.
 - **Urine:** RBC's, WBC's, casts and protein in renal involvement.
 - **Renal biopsy:** Indicated in $\downarrow$ renal function, heavy proteinuria or nephrotic.
May show any pathology of renal diseases (see later)
- **Differential diagnosis:**
 - **Skin rash:** Other causes of purpura.
 - **Arthritis:** Other causes of arthritis
 - **GIT:** Other causes of abdominal pain and bleeding.
 - **Renal:** GN & Nephrotic.
- **Treatment:**
 - **NSAID** → for arthritis
 - **Corticosteroids** → for GIT bleeding, CNS involvement and scrotal swelling.
 - **In Renal** → manage as glomerulonephritis (fluid balance, ttt of hypertension, ..).
- **Prognosis:**
 - Spontaneous recovery is the rule, renal failure rare, death very rare

B- HEMOPHILIAS

Definition:

Inherited blood diseases resulting from impairment of coagulation mechanisms. The most important types are • Hemophilia A (classic hemophilia) • hemophilia B (Christmas disease) • Hemophilia C • Vascular hemophilia (Von Willebrand disease)

Hemophilia A (classic hemophilia)

■ Aetiology: XR disorder resulting from severe deficiency of factor VIII C.

Factor VIII consists of 2 parts: VIII C = clotting part and VIII Ag = antigenic part.

- According to plasma level of F VIII C hemophilia can be classified into:

- 1- **Severe hemophilia:** F VIII C < 1% of normal (spontaneous bleeding).
- 2- **Moderate hemophilia:** F VIII C 1-5% of normal (bleeding from mild trauma).
- 3- **Mild hemophilia:** F VIII C 6-30% of normal (bleeding from severe trauma).
- 4- **Carrier State:** Clinically normal female with F VIII C 40-60% of normal.

■ Clinical picture:

- 1- **Prolonged bleeding after minor surgical procedures** (e.g. circumcision).
- 2- **Skin bleeding:** (Ecchymosis or hematoma) but no petichae.
- 3- **Mucus membrane bleeding:** Gum bleeding, epistaxis and dental bleeding.
- 4- **Internal bleeding:** The most severe is IC Hge after mild trauma to the head.
- 5- **Hemoarthrosis:** Bleeding into the joints (large joints of LL more than UL) later ankylosis and fibrosis of the joints may occur.
- 6- **Hematomas:** Hematomas are common in muscles and S.C. tissues.
- 7- **Hematuria:** Rare presentation.

■ Investigations:

1- Diagnosis of the patient:

- = Phase (I) defect.
- + Prolonged clotting time and Normal bleeding time.

2- Ante natal diagnosis:

- Determination of F VIII Ag & F VIII C in fetal blood sample taken by fetoscopy.
- Direct gene mutation analysis is the most accurate test for carrier detection and prenatal diagnosis. FVIII gene intron 22, resulting from an intra-chromosomal recombination is identifiable.

■ Management:

1- Inbetween the attacks:

- * Identification of the cases who are giving special cards and join society of hemophilic disease patients.
- * Avoid trauma, unnecessary surgical maneuvers and salicylates.
- * Recently DDAVP (Desmopressin) is given by nasal inhalation in mild to moderate cases which may increase the blood level of factor VIII.
- * Vaccination against hepatitis B.

II- During bleeding episodes:• **Replacement therapy by:**

- | | | |
|------------------|---|------------------------|
| | - Fresh frozen plasma (↑ F VIII by 10-25%) | } Every
12
Hours |
| <u>Or</u> better | - Cryoprecipitate (↑ F VIII by 50%) | |
| <u>Or</u> better | - Factor VIII concentrate (↑ F VIII by 50 – 100%) | |

• **Antifibrinolytic therapy:** e.g. E-aminocaproic acid is used to stabilize a clot by inhibiting the normal process of clot lysis by the fibrinolytic system.

• **Management of special cases:**1- **Hemarthrosis:**

- Local application of cold and pressure.
- Initial immobilization followed by passive exercise to prevent joint stiffness.
- Replacement therapy.

2- **Muscle hematoma:**

- Local cold and pressure
- physiotherapy
- Replacement therapy.

3- **Hematuria:**

- Prednisone 2 mg/kg/day for 2 days.

■ **Complications:**I- **Of bleeding:**

- Joint stiffness and deformities.
- Muscle atrophy
- Sequelea of ICH.

II- **Of treatment:**

- 1- Complications of repeated transfusion (see before)
- 2- Factor VIII inhibitors: 5-10% of hemophiliacs develop antibodies against factor VIII ⇒ Refractory to TTT. It can be measured using Bethesda unit of inhibition.

Treatment:

- **Desensitization programs:** in which high doses of factor VIII are infused in an attempt to saturate the antibody.
- **Immunosuppressive drugs , rituximab.**
- **Recombinant factor VII a (Novoseven)** to treat bleeding episodes.

■ **Prognosis:**

With treatment, good outcome is expected but bad prognosis in frequent trauma and the development of F VIII inhibitors or ICHge (rare).

Hemophilia B (Christmas disease)

- * Similar to hemophilia A with the following differences:
- * XR disease but less common (1/5) in incidence than hemophilia A.
- * Same C/P but milder.
- * Same investigations but the deficient factor will be factor IX not VIII.
- * The same ttt but factor IX concentrate (konyne) which contains (II, VII, IX, X) is given instead of factor VIII concentrate every 24 hours (not 12 hours as factor VIII) as the half life of factor IX is 24 hrs.

Vascular hemophilia (Von Willebrand disease)

■ Aetiology:

AD disorder chch by deficiency of both components of F VIII.

1- F VIII C $\Rightarrow$ impairment of coagulation process.

2- F VIII Ag (important for platelet adhesion) $\Rightarrow$ impairment of platelet function.

■ Clinical picture:

* Abnormal bleeding after minor trauma esp. gum, nose & surgical procedures.

* Menorrhagia is common but hemarthrosis is very rare.

Clinical types:

a- **Type 1 VWD** is the most common form and accounts for 85% of cases. Due to deficiency of VWF.

b- **Type 2 VWD** abnormal VWF

c- **Type 3:** homozygous and serious form.

■ Investigations:

1- Prolonged bleeding time and defective platelet adhesion with normal platelet count.

2- Phase (I) defect in coagulation + prolonged clotting time + $\downarrow\downarrow$ both F VIII Ag and F VIII C.

■ Treatment: Replacement therapy by: plasma & cryoprecipitate, f VIII or DDAVP.

■ Prognosis:

- Bleeding problems begin early in life and gets milder with advanced age.
- Normal life expectancy.

C- DISSEMINATED INTRAVASCULAR COAGULATION (DIC)

- **Definition:** Wide spread activation of clotting factors all over the body resulting in:
 - 1- Thrombosis and ischaemia of different vessels.
 - 2- Consumption of coagulation factors → bleeding.
 - 3- Microangiopathic hemolytic anemia and thrombocytopenia.

- **Incidence:** 1: 10.000

- **Aetiology:**

Many diseases may attribute to the wide spread activation of coagulation system but the entire mechanism is not known, however the PPF may be:

- Sepsis (esp. meningococcaemia)
- Tumours (esp. leukaemia)
- Incompatible blood transfusion.
- Anaesthesia
- Severe tissue damage (shock, hyperthermia, dehydration and burns)

- **Clinical picture:**

- 1- Manifestations of the cause.
- 2- Hemorrhagic manifestations: (Purpura, ecchymosis, bleeding from puncture sites).
- 3- Thrombotic manifestations: Infarction or gangrene in skin, subcutaneous tissues, extremities or the kidney.
- 4- Severe anemia and shock.

- **Investigations:**

- 1- Investigations for the cause.
- 2- Anemia and thrombocytopenia → (↓ platelet and ↑ bleeding time).
- 3- Consumption of coagulation factors (Defective all phases of coagulation esp. prolonged P.T. and P.T.T.).
- 4- ↑↑ fibrin degradation products (FDP's) and its by-product D-dimer.

- **Treatment:**

- 1- Aggressive management of the cause.
- 2- Plasma or whole blood transfusion.
- 4- Heparin usage in thrombosis is controversial.

- **Prognosis:**

- Depending on the cause and the extent of spread of coagulations.
- Generally poor prognosis.

CHAPTER (II)

ONCOLOGY

I- LEUKEMIAS

Leukemia is malignant uncontrolled proliferation of WBC's which is the commonest malignancy in Pediatrics.

☆ Aetiology:

- ✦ Most cases of leukemias are idiopathic but leukemia has ↑ incidence with:
 - 1- Chromosomal anomalies: e.g. Down syndrome.
 - 2- Excess chromosomal breakage: e.g. Bloom syndrome, Fanconi anaemia and Ataxia telangiectasia.
 - 3- As a 2ry tumour after irradiation or chemotherapy.

☆ Classification of leukemias:

- 1- Acute lymphoblastic leukemia (ALL) → 75 %.
- 2- Acute myeloid leukemia (AML) → 20%.
- 3- Chronic myeloid leukemia (CML) → 5%.

ACUTE LYMPHOBLASTIC LEUKEMIA (ALL)

☆ Incidence:

- ✦ Age → 3-5 years is the peak age.
- ✦ Sex → male > female.
- ✦ Race → white > black races

☆ Classification of ALL:I- Morphological [FAB classification].

- ✦ L1 (85%) → small lymphoblasts (Best prognosis).
- ✦ L2 (14%) → large lymphoblasts (Fair prognosis).
- ✦ L3 (1%) → cells with cytoplasmic vacuolization (Worst prognosis).

II- Immunological classification:

Through the use of monoclonal antibodies directed against cell surface protein and cytoplasmic protein (CD, cluster of differentiation) of malignant cells. Through this ALL classified into B&T based on the normal pattern of lymphocyte ontology.

According to surface biochemical markers on the blast cells:

- ✦ Common ALL → 70% (excellent prognosis.)
- ✦ Pre B cell leukemia → 15% (fair prognosis).
- ✦ T cell leukemia → 20% (poor prognosis).
- ✦ B cell leukemia → 1-2% (poor prognosis).

III- Chromosomal classification:

According to chromosomal abnormalities of leukemic cells (translocation).

☆ Clinical manifestations:

1- Non specific manifestations:

Early features of the disease e.g. fever, anorexia, loss of weight, . .
(due to hypercatabolism).

2- Manifestations of bone marrow infiltration:

⊕ Thrombocytopenia → bleeding and purpura.

⊕ Anaemia → pallor, irritability,

⊕ Neutropenia → recurrent infections.

3- Manifestations of organ infiltration:(especially in T-cell type).

⊕ Hepatosplenomegaly and lymphadenopathy.

⊕ Bone pain and arthralgia esp. tender sternum.

⊕ ↑ ICT (if CNS infiltration). ⊕ Spinal cord infiltration with paraplegia.

⊕ Painless testicular swelling (if testicular infiltration).

☆ Investigations:

1- CBC:

⊕ Anaemia: (↓ Hb, ↓ RBC's).

⊕ Thrombocytopenia: (↓ platelets).

⊕ WBC's: usually ↑ but may be normal or ↓ but contains abnormal (blast) cells(normally no blast cells in peripheral blood).

2- Bone marrow:

⊕ Hypercellular replaced by leukemic blast cells > 25% (normally blast cells < 5% in B.M.) Lymphoblasts are PAS+ve in clumps.

3- Immunophenotyping:

⊕ To determine the type (B, T type).

4- Investigations for organ infiltration:

⊕ X-ray chest → "for mediastinal mass".

⊕ CSF exam → "for leukemic cells".

⊕ X-ray bone → "for infiltration of bone".

⊕ Liver and kidney functions.

✱ **N.B.** ➤ Tumor lysis syndrome occurs due to rapid breakdown of tumor cell usually with initiation of therapy and is characterized by hyperkalemia, hyperuricemia, hyperphosphatemia and hypocalcemia.

☆ D.D.:1- Other causes of B.M. infiltration:

- ⊕ Lymphoma ⊕ Neuroblastoma ⊕ Rhabdomyosarcoma.

2- Acute myeloid leukemia (AML):

- ⊕ Peroxidase +ve granules .
- ⊕ Sudan black +ve granules. } Are present only in AML (not in ALL).

3- Causes of fever & arthralgia:

- ⊕ Rheumatic fever ⊕ Rheumatoid arthritis

4- Causes of purpura ± bleeding:

- ⊕ ITP ⊕ Henoch Schonlein purpura.

5- Aplastic anaemia:

Features of B.M. infiltration but no other organ infiltration (e.g. No HSM, lymphadenopathy, testicular,)

6- Causes of marked ↑ WBC's in peripheral blood:

e.g. pertussis, IMN, (called leukomoid reaction).

7- Causes of hepatosplenomegaly and lymphadenopathy.☆ Treatment of ALL: (General – specific – course).A- General Measures1- Blood component therapy:

- ⊕ Blood or packed RBC's for anaemia.
- ⊕ Platelet transfusion for severe thrombocytopenia.

2- Treatment of infections by aggressive antibiotic ttt:3- Good nutrition and adequate hydration4- Management of complications of ttt: e.g. allopurinol for hyperuricaemia.5- Leukapheresis in case of leukostasis.B- Specific Measures (Chemotherapy)Treatment Elements1-Induction2-CNS therapy3-Consolidation4-Maintenance Therapy

A) Induction of remission: (for 4 weeks)

- **Pridnisone** : 60 mg/m²/day orally.
- **Vincristine** : 1.5 mg/m²/week IV.
- **Adriamycin** : 25 mg/m²/week IV.
- **L. Asparganase** : (9 doses) intramuscular

This regiment gives remission in 85% of the cases.

* **Criteria of remission:**

- Clinical improvement (no HSM nor LN enlargement)
- CBC : no blasts
- BM : < 5% blasts in normocellular BM
- CSF : no blasts

B) CNS prophylaxis

- Cranial irradiation.: not recommended
- Intrathecal Methotrexate.

C) Consolidation phase: period of intensive therapy to decrease the incidence of relapse with different combination of chemotherapy.

D) Maintenance of remission: for 2-3 Years: The main drugs used are

- 6 mercaptopurine : 50 mg/m²/day orally.
- Methotrexate: 20 mg/m²/week I.V.

☞ **N.B.: Bone marrow transplantation:** in poor responder and relapse.

⊕ **Complications of chemotherapy:****1- General complications:**

- Bone marrow suppression (Pancytopenia).
- Tumour lysis syndrome (↑ K, ↑ uric acid, ↑ Ph & ↓ Ca).

2- Specific complications:

- Adriamycin (cardiomyopathy).
- Methotrexate (renal toxicity & stomatitis).
- Cyclophosphamide (Hgc cystitis).
- Oncovin (Peripheral neuritis & ileus)
- Prednisone (Complications of steroid ttt).

C- Course

- * The aim of treatment is to achieve long remission (clinical and laboratory).
- * Relapse is reappearance of the disease either →
 - 1-Isolated BM relapse:>25% blast in BM
 - 2-Isolated extramedullary Relapse:less than 5% blast I the BM and blast cells in other sites as tests, CNS and others
 - 3-Combined relapse. extramedullary and > 5% blast in BM.
- * In relapse re-induction of treatment with more aggressive chemotherapy is indicated and BM transplantation.

N.B. Treatment of mature B-cell leukemia = treatment of Non-Hodgkin's lymphoma.

☆ **Prognosis of ALL:**

	Good prognosis	High risk (bad prog.)
* Sex	→ female	→ male
* Age	→ 2-8 years	→ < 2 and > 10 years
* Initial WBC's	→ < 50.000 / cc	→ > 50.000 / cc
* Type of cells	→ common ALL	→ T
* Mediastinal mass	→ No	→ +
* CNS infiltration	→ No	→ +
* Testicular	→ No	→ +
* Organomegaly	→ No	→ +

ACUTE MYELOID LEUKEMIA (AML)

☆ **Incidence:**

20% of cases of leukemia with equal sex incidence, race distribution and age from 1-10 years

☆ **Classification:** (FAB classification)

From M1 to M7 according to the morphology of malignant cells.

- ✪ M1 Myeloblasts with no maturation.
- ✪ M2 Myeloblasts with some maturation (chloroma is common)
- ✪ M3 Pro myelocytic (DIC is common)
- ✪ M4 Myelomonocytic
- ✪ M5 Monocytic (gingival hyperplasia is common)
- ✪ M6 Erythroleukaemia.
- ✪ M7 Megakariocytic

☆ **C/P:** As ALL but

- * Spleen affected > liver
- * Rare testicular involvement.

☆ **Investigations:**

As ALL except immunophenotyping.

☆ **D.D.:** As ALL

☆ **Treatment:**

- 1- Induction Phases(to attain remission)
The common drugs used Cytarabine, doxorubicin and etoposide.
- 2- Post-remission consolidation/intensification: postremission therapy consist of varying numbers of courses of intensive chemotherapy and / or allogeneic bone marrow transplantation.
- 3- Maintenance therapy is not part of most pediatric AML protocol.

☆ **Prognosis:**

- ◆ Children have better prognosis than adults.
- ◆ ALL is better than AML: (5 years survival 80% in ALL and 50% in AML)

II- LYMPHOMAS

	Hodgkin lymphoma (HL)	Non Hodgkin lymphoma (NHL)
* Incidence	- 30% of lymphomas. - Male > female (3:1). - Peak age 15-34 years.	- 70% of lymphomas. - Male > female (3:1). - Peak age 5-15 years.
* Cause Both unknown but ↑ risk with:	- Viral infection e.g EBV. - Immunodeficiency syndromes.	- Viral infection e.g EBV esp. in African type (Burkitt's lymphoma) - Immunodeficiency syndromes.
* Histological Classification	• 4 types according to the ratio between lymphocytes (Reed-Sternberg cells) and reticular fibers. 1- <u>Lymphocyte predominant</u> (10%) → best prognosis. 2- <u>Nodular sclerosing type</u> (50%) → next favorable. 3- <u>Mixed cellularity type</u> (40%) → bad prognosis. 4- <u>Lymphocyte depletion</u> (<1%) → worst prognosis	(I) According to aggressiveness: - High grade (NHL) 90% - Intermediate grade (NHL) - Low grade (NHL) (II) Immunological classification - B-cell (NHL) → 40% - T cell (NHL) → 40% - Non B-non T → Rare
* Staging:	1- Stage I: One L.N. or one extralymphatic tissue. 2- Stage II: More than one LN or extralymphatic tissue on same side of the diaphragm. 3- Stage III: As stage II but on both sides of the diaphragm. 4- Stage IV: Diffuse or disseminated disease.	1- Stage I: Single mass (not abdomen or mediastinum) 2- Stage II: More than one mass on same side of the diaphragm or 1ry abdominal tumour. 3- Stage III: More than one mass on both sides of the diaphragm or 1ry mediastinal tumour or extensive abdominal tumour. 4- Stage IV: One of the above + CNS or B.M. involvement.
* C/P:	1- Constitutional manifestations: - Intermittent fever (Pel Ebsstein). - Weight loss, anorexia. - Night sweating. 2- Nodal involvement (> 90%) • Painless, firm, discrete, rubbery early single then becomes matted, commonly cervical LN or supraclavicular ± inguinal, axillary,... • Mediastinal LN ++ may lead to mediastinal syndrome. • Mesenteric LN ++ → Abd. mass. 3- Extranodal involvement (Rare) • B.M. → pancytopenia. • Spleen → splenomegaly. • Liver → hepatomegaly. • CNS → mass → cord compression	1- Constitutional manifestations: - Uncommon 2- Nodal involvement: • L.N. on head & Neck (20%) → Painless swellings. • Mediastinal mass (30%) → Mediastinal syndrome. • Abdominal mass (40%) → Abdominal pain, vomiting, mass. 3- Extranodal involvement (common) • Bone → bone pain. • Skin → nodules. • Other sites → as Hodgkin

	Hodgkin lymphoma	Non Hodgkin lymphoma (NHL)						
* Investigations	<u>1- L.N. biopsy & exam.</u> <u>2- Investigations B.M. infiltration ⇒</u> • Pancytopenia in CBC • Infiltration of BM in BM biopsy <u>3- Investigations for other organ involvement:</u> • X-ray chest. • CT brain or vertebral column. • Sonar abdomen <u>4- Staging laparotomy:</u> • For: - LN samples - Liver biopsy. - Splenectomy.	1- 2- As Hodgkin Lymphoma 3- <u>4- Immunophenotyping:</u> • For B, T or Null types						
* D.D.:	• Causes of lymphadenopathy. • Hodgkin from Non-Hodgkin lymphomas							
* Treatment:	Two modality of therapy <u>1- Chemotherapy:</u> Either • MOPP derivative: Mecllorethamine, oncovine, procarbazine and prednisone. • ABVD derivative: Adriamycin, Bleomycin, Vinblastine and Dacarbazine. <u>2-adiotherapy</u> <u>3-Management of complications:</u> • Antibiotics for infection. • Blood transfusion.	<u>2-Chemotherapy: according to the type of NHL</u> • common chemotherapy used: Cyclophosphamide. High dose methotrexate. Oncovin. Ara-C + CNS prophylaxis (as ALL) <u>3- Management of complications</u> As Hodgkin						
* Prognosis:	• 5 years survival rate:<table><tr><td>Stage</td><td></td></tr><tr><td>I, II</td><td>> 90%</td></tr><tr><td>III, IV</td><td>> 70%</td></tr></table> • Hodgkin lymphoma is better than non Hodgkin lymphoma		Stage		I, II	> 90%	III, IV	> 70%
Stage								
I, II	> 90%							
III, IV	> 70%							

(III) DEVELOPMENTAL TUMOURS**WILM'S TUMOUR "NEPHROBLASTOMA"**☆ **Incidence:**

- ⊕ The commonest renal tumour in pediatrics.
- ⊕ Peak age: around 3 years.
- ⊕ Sex: equal sex incidence.

☆ **Types:**

- ⊕ **Sporadic form:** Common, usually unilateral, not associated with other anomalies.
- ⊕ **Familial form:** Very rare, may be bilateral, commonly associated with aniridia, hemihypertrophy or ambiguous genitalia.

☆ **Staging:**

- ⊕ **Stage (I):** → Tumour confined to one kidney.
- ⊕ **Stage (II):** → Tumour extends beyond the kidney but can be completely excised.
- ⊕ **Stage (III):** → Tumour which shows residual abdominal extension after surgery.
- ⊕ **Stage (IV):** → Haematogenous spread (mainly lung & liver).
- ⊕ **Stage (V):** → Bilateral tumour at the time of diagnosis.

☆ **C/P:**

- 1- **Abdominal mass** (Huge, rarely cross the midline) is the commonest presentation.
- 2- **Abdominal pain**
- 3- **Hypertension** ($\frac{1}{2}$ of cases).
- 4- **Haematuria** (uncommon)

☆ **Investigations:**

- 1- **To detect the tumour:** Abdominal sonar / CT / MRI / Biopsy.
- 2- **To detect spread:** Chest x-ray / liver scan / CT brain.

☆ **Treatment:** 3 modality of therapy

- 1- **Chemotherapy** : drug used actinomycin, vincristin and doxorubicine according to the stage of the disease
- 2- Surgery → **Nephrectomy**.
- 3- **Radiotherapy** : according to the stage, pathology and postoperative complication

☆ **Prognosis:**

- **Stage I, II, III** : → 5 years survival rate 80 – 90%.
- **Stage IV** : → 5 years survival rate < 70%.
- **Stage V** : → Poor prognosis.

NEUROBLASTOMA

☆ Incidence:

- The commonest solid tumour outside CNS.
- Age: 50% of cases occur < 2 years age (the commonest infant & neonatal tumour) & 85% before 6 years of age.
- Sex: Slight commoner in male.

☆ Neuroblastoma may arise from any site containing neural crest cells:

- 35% → Adrenal medulla.
- 35% → Abdomen (outside adrenal medulla).
- 25% → chest (mediastinal).
- 5% → Other sites (e.g. head & neck, pelvis).

☆ Staging:

- Stage (I) :→ Tumour confined to an organ.
- Stage (II) :→ Tumour extend beyond the organ but not cross the midline.
- Stage (III) :→ Tumour crosses the midline.
- Stage (IV) :→ Remote disease (e.g. bone, organs, LN,...).
- Stage (IVs) :→ Stage I or II + remote disease to:

♣ Liver

♣ Skin

♣ BM (not bone)

This stage carry good prognosis.

☆ C / P:

Multiple presentations may occur due to different sites of involvement & high incidence of metastasis (50% of cases have remote metastasis at diagnosis).

- Abdominal mass (may cross the midline).
- Mediastinal mass (mediastinal syndrome).
- Proptosis.
- Secretory diarrhea (due to ↑ vasoactive substances)
- Hypertension (due to ↑ catecholamines)
- Hepatomegaly
- skin nodules
- pancytopenia .

☆ Investigations:**1- For primary tumour:**

- A- Imaging: Abdominal sonar, CT or MRI.
- B- Biopsy:
- ↑ Vanillyl mandilic acid in urine (VMA) is a good screening test
- MIBG scan.

2- To detect metastasis:

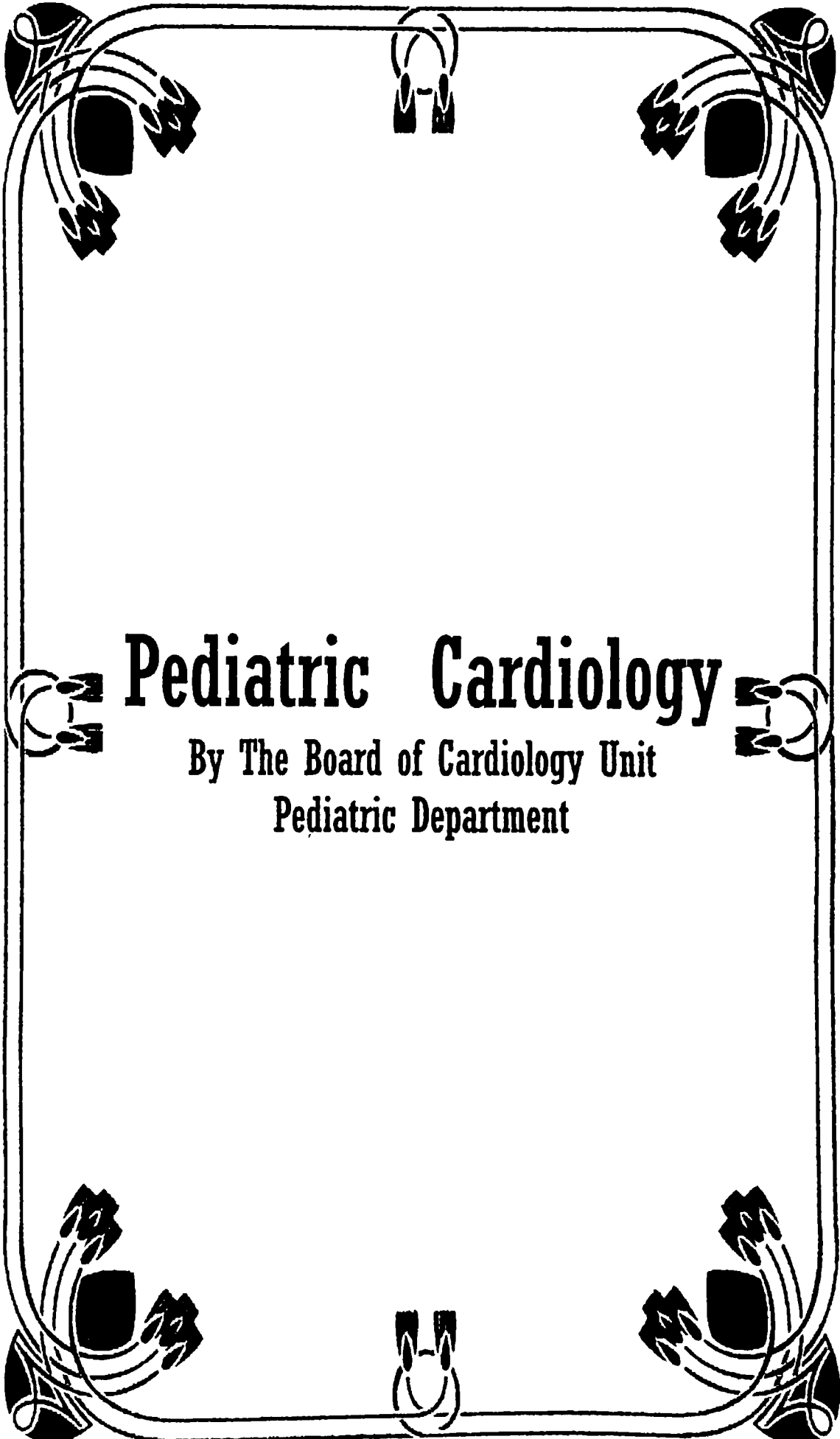
- 1- Bilateral BM biopsy
- 2- Bone scan

☆ Treatment:

Surgery + Radiotherapy + combined chemotherapy

☆ Prognosis:

- Young age better prognosis than older (spontaneous regression may occur < 1 years old).
- 5 years survival rate < 40% & may be < 5% in stage IV.



Pediatric Cardiology

By The Board of Cardiology Unit
Pediatric Department

CHAPTER (XI)

CARDIOLOGY

Diagnosis Of Cardiac Case**I- Suspect cardiac disease from symptoms of:****1- Pulmonary venous congestion:****a- In infants:**

- ☆ poor feeding (dyspnea on suckling).
- ☆ recurrent chest infections.
- ☆ recurrent heart failure.
- ☆ growth retardation

b- In older children:

- ☆ exertional dyspnea.
- ☆ cough (exertional & positional)
- ☆ haemoptysis.

2- Systemic venous congestion:

- ☆ enlarged tender liver
- ☆ dyspepsia
- ☆ oedema

3- low cardiac output:

- ☆ dizziness.
- ☆ transient syncopal attacks
- ☆ anginal chest pain
- ☆ easy fatiguability (exercise intolerance)

4- Cyanosis & hypercyanotic spells**II- Which cardiac chamber is enlarged?****1- Precordial examination (inspection/palpation/percussion)****LVH:**

- ☆ Apex is localized and shifted down & out

RVH:

- ☆ Precordial bulge
- ☆ Apex is diffuse & shifted out.
- ☆ left parasternal pulsation.
- ☆ Epigastric pulsation

2- Chest X-ray**3- ECG****4- Echocardiography & catheterization**

III- What is the organic lesion:

1- Auscultation:

i. Heart sound:

1- First heart sounds (S1):

- ☆ Due to closure of atrio ventricular valves.
- ☆ Heard over apex & tricusped areas.
- ☆ Accentuated in atrio ventricular valves stenosis.
- ☆ Muffled in atrio ventricular valves regurge.

2- Second heart sound (S2):

- ☆ Due to closure of semilunar valves.
- ☆ Composed of aortic component (A2) & pulmonary component (P2).
- ☆ Heard over aortic area & pulmonary area.
- ☆ Usually both components & split during inspiration & unite during expiration.
- ☆ Accentuated in hypertension.

3- Third heart sound:

- ☆ Due to rapid filling of the left ventricle in early diastole
- ☆ May be heard normally in healthy children.
- ☆ Heard mostly in congestive heart failure.

4- Fourth heart sound:

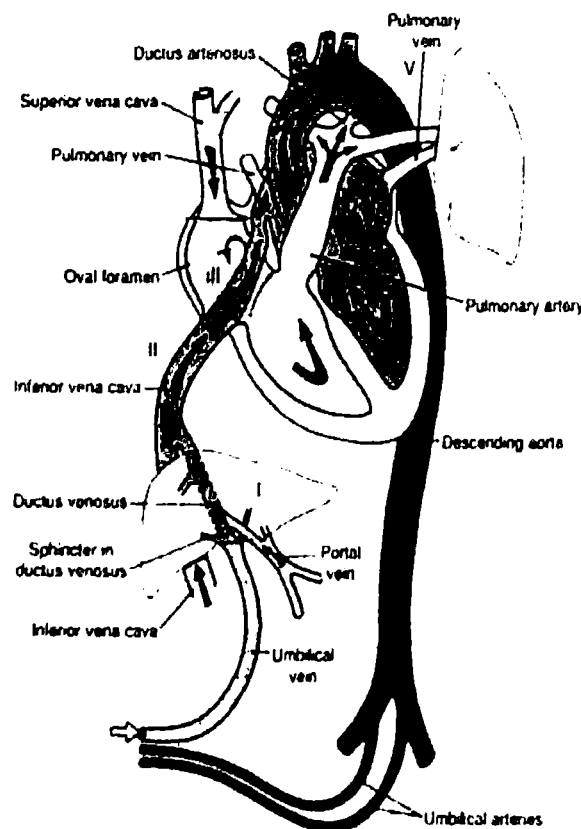
- ☆ Due to forcible atrial contraction.
- ☆ Always abnormal (due to decreased ventricular compliance).

ii. Study of murmurs:

- 1- Timing: systolic or diastolic or continuous
- 2- Site of maximum intensity & propagation.
- 3- Intensity classified as:
 - ☆ Grade I : Soft, heard with difficulty.
 - ☆ Grade II : Soft, easily heard.
 - ☆ Grade III : Loud without thrill
 - ☆ Grade IV : Loud with thrill..
 - ☆ Grade V : Louder with thrill.
 - ☆ Grade VI : Loud + thrill + heard with stethoscope off the chest.
- 4- Quality: Harsh, soft, musical:

FETAL CIRCULATION

- For the fetus the placenta is the site of gas and nutrient exchange ,so the lungs do little work
- Right ventricle RV & left ventricle LV contribute equally to the systemic circulation and pump against similar resistance
- Shunts are necessary for survival*
 - ductus venosus (bypasses the liver)
 - foramen ovale (Rt→Lt atrial level shunt)
 - ductus arteriosus (Rt→Lt arterial level shunt)
- Oxygenated blood from placenta returns to the fetus via umbilical vein(only one vein) →Blood bypass the liver via Ductus venosus to IVC→ Mix with blood from the lower limbs →This blood enters the RA, Pressure in the RA > LA. Major part of this blood pass via the Foramen ovalae to the LA→ Mix with deoxygenated blood from the lungs at LA → goes to the LV → the Aorta → Coronary & carotid arteries to supply the heart and the brain with relatively well oxygenated blood.
- Deoxygenated blood from the SVC flows to RA → RV → pulmonary trunk. Major part of its blood pass directly through Ductus arteriosus → the descending aorta to supply the lower half of the body .
- Blood returns to the placenta via 2 umbilical arteries to repeat the circuit.



Circulatory Changes At Birth:

-With the first few breaths at birth → lungs expand → ↓ pulmonary vascular resistance → ↑ pulmonary blood flow → ↑ LA pressure.

-Removal of the Placenta → ↓ venous return to RA → ↓ RA pressure. This together with ↑ LA pressure → Closure of the Foramen ovale functionally.

-Closure of

- Umbilical artery
- Umbilical vein
- Ductus venosus
- Ductus arteriosus
- Foramen ovale

CONGENITAL HEART DISEASES

Epidemiology :

- ☆ Prevalence: 0.5-0.8% of live births (8/1000).
- ☆ Leading structural malformation in infants.
- ☆ 10-15% have extracardiac anomalies (VACTERL)
- ☆ Gender differences :
 - ASD, VSD, PDA & Pulmonary stenosis are more in girls.
 - Aortic Stenosis & Coarctation of aorta, are more in boys.

Etiology

☆ Unknown

☆ Multifactorial inheritance

☆ Genetic (Chromosomal/Single gene)

- Trisomies 13, 18, 21 → AVSD, VSD, ASD, TOF)
- Monosomy X (Turner's syndrome): → A Co.)
- 22q11 microDeletion (DiGeorge syndrome): Conotruncal abnormalities (TOF & TGA)
- Single gene defects :
 - Noonan's syndrome → PS
 - Marfan syndrome → AR, MR)

☆ Teratogens (Maternal disorders / Drugs)

- Maternal disorders
- Rubella → PS, PDA.
- Systemic Lupus Erythematosus → congenital heart block.
- Diabetes Mellitus → HOCM, VSD.
- Fetal alcohol syndrome → VSD, ASD, TOF.
- Drugs: Warfarin, Lithium, Phenytoin, valproate, Retinoic acid.
- Ebstein anomaly has been linked to Lithium intake during pregnancy.

Classification of Congenital Heart Diseases.

Acyanotic CHD

-Lt→Rt shunts lesions:

VSD

ASD

PDA

AVSD (common AV canal)

-Obstructive lesions:

Pulmonary stenosis

Aortic stenosis

Coarctation of Aorta

Cyanotic CHD

(Rt→Lt shunt)

-CHD with ↑ pulmonary blood flow:

Transposition of the Great Arteries

Total Anomalous Pulmonary Venous Connection

Truncus Arteriosus

-CHD with ↓ pulmonary blood flow:

Tetralogy of Fallot

Tricuspid Atresia

Pulmonary atresia

Ebstein's Anomaly

Acyanotic Lt→Rt Shunts lesions – General Points

PDA & VSD	ASD
♣ Presents in infancy with heart failure, murmur and poor growth ♣ Left heart enlargement (LHE) ♣ Transmits flow and pressure	♣ Presents in childhood with murmur or exercise intolerance ♣ Right heart enlargement (RHE) ♣ Transmits flow only
AVSD can present as either depending on size of ASD & VSD component (AVSD or / primum ASD presents earlier)	

Cyanotic CHD – General Points

↑ PBF	↓ PBF
♣ Presents more often with heart failure (except TGA) ♣ Pulmonary congestion worsens as neonatal PVR lowers ♣ O₂ Saturations can be 93-94% if there is high PBF	♣ Presents more often with cyanosis ♣ Severe pulmonary oligemia → recurrent cyanotic spells. ♣ Closure of PDA may worsen cyanosis

Presentations Of CHD:

- Antenatal cardiac US
- Detection of murmur
- Cyanosis
- Respiratory distress
- Heart failure
- Shock

Heart murmurs:

Ejection systolic murmur	Pansystolic murmur	Continuous murmur
AS, PS, ASD.	VSD, MR, TR	1.PDA
Innocent murmur		2.Venous hum

Hallmarks of innocent (functional) murmurs:

- soft
- Systolic, No diastolic component
- Confined to small area, left sternal edge
- No radiation
- No parasternal thrill
- Normal heart sounds, No added sound
- Asymptomatic patient
- N.B: There may absence of murmur in severe CHD like PDA, large VSD esp. in neonates with high PVR

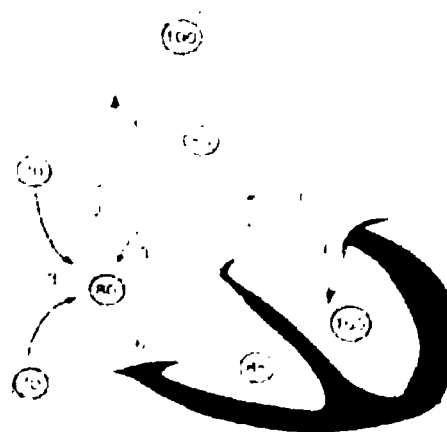
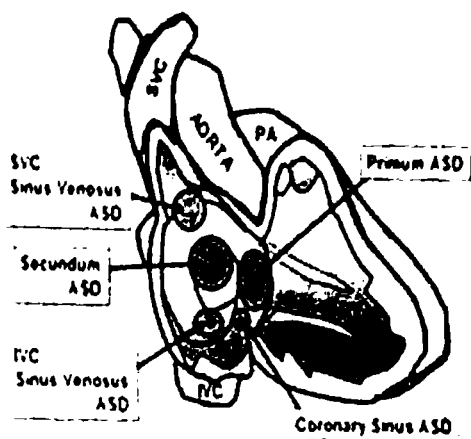
Hallmarks of Cardiac Cyanosis

- Central cyanosis
- Does not respond to oxygen
- Does not respond to ventilation
- Usually no respiratory distress

Three types exist :

- **Primum ASD:** in the lower portion of the interatrial septum.
- **Secundum ASD:** in the mid portion of the interatrial septum.
- **Sinus Venosus ASD:** close to the entrance of SVC, often associated with Partial Anomalous Pulmonary Venous Return.

*The most common is the secundum type, followed by primum type.



Types and Physiology of atrial septal defect (ASD). Circled numbers represent oxygen saturation values

Symptoms: None in childhood, arrhythmias in the 3rd decade

Clinical signs:

- include a 2-3/6 Systolic Ejection Murmur at the ULSB and a fixed wide split S2 (due to relative pulmonary stenosis).
- A large ASD causes enlargement of both right atrium & ventricle.

ECG:

Secundum ASD → right axis deviation and RBBB

Primum ASD → left axis deviation (superior axis)

Echocardiography: Diagnostic

Natural History: Small ASDs close spontaneously, Unrepaired large defects may lead to arrhythmias and pulmonary vascular obstructive disease in the 3rd and 4th decades.

Treatment : Surgical vs. transcatheter closure (secundum type).

VENTRICULAR SEPTAL DEFECT (VSD)

- *This is the most common form of CHD
- *The VSDs are subdivided according to the part of the septum they occur in
 - Muscular VSD,
 - Perimembranous VSD,
 - Inlet VSD,
 - Outlet VSD,



Physiology of atrial septal defect (ASD). Circled numbers represent oxygen saturation values

Symptoms:

- With a small defect, no symptoms.
- With a large defect there may be congestive heart failure (usually at 6-8 weeks), pulmonary infections and delayed growth.

Clinical signs :

- Loud 4-5/6 , harsh pansystolic murmur on the left parasternal area propagated all over the precordium
- middiastolic rumble and a loud P2.
- A large VSD causes LA & LV enlargement.

ECG: Left ventricle / or biventricular hypertrophy.

Echocardiography: Diagnostic

Natural history : Small VSDs close spontaneously depending on the site. Unrepaired large defects may lead to Eisenmenger's syndrome.

Treatment:

- Prophylaxis against infective endocarditis
 - medical: Diuretics, digoxin and afterload reducing agents are used prior to surgery if needed.
 - Surgical: Large VSDs are closed surgically usually at about 4- 6 months of age.
- Transcatheter closure in selected cases.

Patent Ductus Arteriosus (PDA)

- *It is a vascular connection between the pulmonary artery and the aorta just distal to the origin of the great vessels.
- *Very common in preterm babies.
- *Usually closes in the first 2 weeks of life.



Symptoms :

- a) None if small
- b) If large can cause CHF at 6-8 weeks in a term infant
- c) In a preterm baby increasing respiratory support usually occurs after day 3 of life.

Signs:

- Systolic murmur in a newborn and a continuous machinery "train in a tunnel" murmur in an older child. Best heard below the left clavicle.
- A large PDA causes LA and LV enlargement.

ECG: LA and LV hypertrophy.

Echocardiography: Diagnostic

Treatment :

- In a preterm: it can be closed medically using IV indomethacin / or oral Ibuprofen.
- In a term baby if still open at 3 months of age:
- Transcatheter closure by coil or duct occluder is the method of choice.
- Surgical ligation for a large PDA.

N.B: Diuretics, digoxin and afterload reducing agents are used prior to surgery - if needed.

COARCTATION OF THE AORTA

- Anatomical defect:

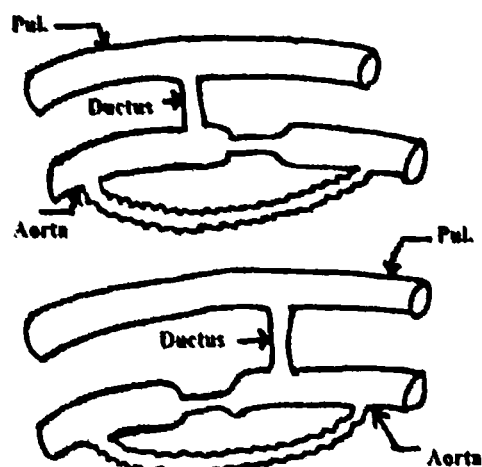
Narrow Segment of the Aorta:

1- Ductal and post ductal:

Are the most common types

2- Preductal:

Associated with other congenital anomalies and associated with differential cyanosis (Blood pass from pulmonary to aorta leading to LL cyanosis while upper limb and face are not cyanosed as they are supplied before the duct).



- Haemodynamics:

Obstruction to the Aortic flow:

⊙ ↑↑ pressure before the narrow segment.

⊙ ↓↓ pressure after the narrow segment.

The lower part of the body is supplied through collaterals between the proximal and distal parts of the Aorta.

Lt. ventricular hypertrophy → later left vent. failure (Low COP and pulmonary congestion)

Manifestations: "May be asymptomatic for long period"

- Congestive pulmonary manifestations.
- ↓ COP manifestation in the lower half of the body.
- Manifestations of hypertension in the upper half of the body.
- Disparity in pulse (Prominent in UL than LL).
- Disparity in BP (More in UL than LL).
- Ejection systolic murmur (apex, Lt. sternal border *or* interscapular → characteristic) due to blood flow through the co-arcating segment and opened collaterals.

Chest X-ray:

- May be normal ± LV ++.
- Rosler sign (Rib notching in lower border of the ribs from the 3rd rib downward) → due to the pressure of collaterals on the ribs.

ECG: → Lt. vent. ++

ECHO: → Diagnostic but ECHO Doppler is the best.

Catheterization: → to assess the pressure gradient (Pre-operative) or if not diagnosed by ECHO.

Complications:

- 1- CHF (post-ductal coarctation is the commonest cause of CHF in neonates)
- 2- Intracranial hge (due to hypertension)
- 3- Infective endocarditis.

Treatment:

- Medical:
 - TTT of CHF.
 - TTT of hypertension
 - Prophylaxis against infective endocarditis.
- Surgical: Resection of the segment (coarctotomy) followed by end to end anastomosis.

CONGENITAL CYANOTIC HEART DISEASES

- ✱ The most common is Tetralogy of Fallot (TOF) then Transposition of Great Arteries (TGA).

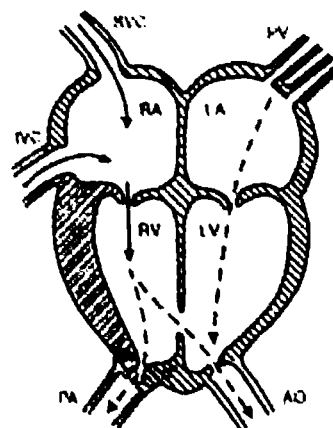
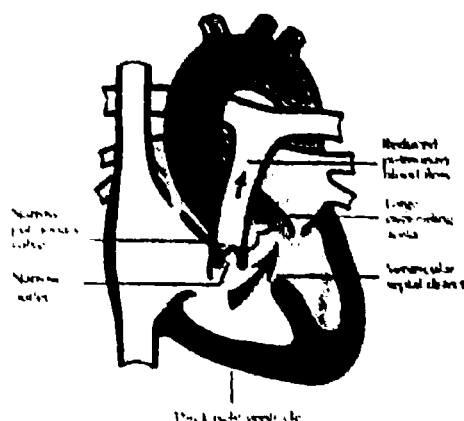
Cyanotic congenital HD with ↓ pul. blood flow

- ✧ This group is chch by:
 - Common cyanotic spells (Rare heart failure).
 - Diminished second heart sound (↓ S2).
 - Lung oligoemia in X-ray chest.
- ✧ The typical example for this group is TOF.

A- TETRALOGY OF FALLOT

Anatomical defect:

- 1- Pulmonary stenosis: usually infundibular but may be valvular or mixed.
- 2- Rt. vent. hypertrophy: usually mild.
- 3- Ventricular septal defect: usually big.
- 4- Overriding Aorta: receives blood from both vent.



Haemodynamics:

- 1- During Rt. ventricle contraction, most of the blood will be pushed to the left ventricle through the big VSD and few amount is pushed through the stenotic pulmonary valve.
- 2- The net result will be:
 - Mixed blood in the aorta → (cyanosis)
 - ↓ Pul. flow → ↓ oxygenation and pulmonary oligoemia.
 - ↓ O₂ tension → hypoxia → bone marrow ++ → polycythaemia.
 - The pul. flow will be maintained by collateral circulation or PDA.

Clinical features:**1- Central Cyanosis:**

- Normally appears after 6 months age
- Early or at birth in severe pulmonary stenosis.
- Late or absent cyanosis in mild pul. stenosis (Pink Fallot).

2- Squatting position:

- Squatting is involuntary position which leads to $\uparrow$ oxygenation of blood by:
 - $\diamond \uparrow$ systemic vascular resistance $\rightarrow \uparrow$ Aortic pressure $\rightarrow$ more blood pass to pulmonary artery to be oxygenated.
 - $\diamond$ Squeezing blood from viscera which is more oxygenated than other parts of the body.

3- Hypercyanotic (blue) Spells:

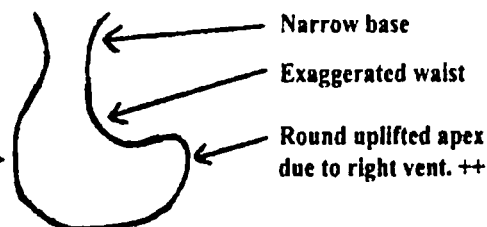
- $\Rightarrow$ Attacks of deepening of cyanosis and respiratory distress in patients with cyanotic CHD esp. TOF as a result of $\uparrow\uparrow$ infundibular pulmonary spasm.
- $\Rightarrow$ Predisposing factors: Irritability, Infection, Iron deficiency.
- $\Rightarrow$ The attack occurs mostly in the morning with disappearance of the murmur.
- $\Rightarrow$ TTT of attack includes:
 - 1- O_2 , Squatting,
 - 2- Morphine 0.1 mg/kg SC ($\downarrow$ irritability).
 - 3- Propranolol 0.1 mg/kg IV ($\downarrow$ infundibular spasm)
 - 4- $NaHCO_3$ 1-2 ml/kg IV (correct acidosis).
 - 5- Ketamine 1.0 mg/kg. IV (in failure of other lines)

4- Clubbing of fingers: After 1-2 yrs (not at birth)**5- Stunted Growth:** In non operated cases.**6- Cardiac examination:**

- $\Rightarrow$ Inspection, Palpation & percussion $\rightarrow$ (Rt. vent. hypertrophy) $\pm$ thrill.
- $\Rightarrow$ Auscultation $\rightarrow$
 - * Single second heart sound.
 - * Ejection systolic murmur on the left 2nd - 3rd space parasternal (of pul. stenosis).
 - * No murmur of VSD is detected.

Investigations:**1- Blood:** Polycythaemia.**2- X-ray chest:**

- Oligaemic lung field.
- Cardiac size: normal
- Typical configuration (Boot shaped heart = coeur en sabot) $\rightarrow$
- Rt. aortic arch in 25% of cases

**3- ECG:** Rt. ventricular hypertrophy**4- ECHO:** Diagnostic**5- Catheterization:** Shows $\Rightarrow \downarrow\downarrow O_2$ tension in the aorta.
 $\Rightarrow \uparrow\uparrow$ Rt. ventricular pressure.

② **Complications:**

- 1- **Cerebral thrombosis** 2ry to polycythaemia.
- 2- **Brain abscess** due to lack of filtration by pulmonary circulation.
- 3- **Pulmonary T.B.** due to oligemic lung.
- 4- **Infective endocarditis.**
- 5- **Congestive H.F.** (Rare) occurs in pink Fallot or 2ry to iron deficiency anaemia.

② **Treatment:**

1- **Medical ttt:**

- TTT of cyanotic spells (see before).
- Avoid **digitalis** (↑ infundibular pul. stenosis) & **dehydration** (↑ risk of thrombosis).
- Iron supplementation to decrease incidence of thromboembolic complications due to relative iron deficiency.
- Prophylaxis against infective endocarditis.

2- **Surgical ttt:**

a- ***Palliative shunt (Artificial PDA):***

- The idea is performing simple operation to create artificial anastomosis between aorta and pulmonary ⇒ more blood is shunted to the lung ⇒ more oxygenation until the infant grows and total correction becomes possible.
- Types:
 - ◊ anastomosis between subclavian artery and pulmonary artery using Gore-Tex conduit (modified Blalock Taussing operation)
 - ◊ anastomosis between ascending aorta and pul. A. (Waterson operation)
 - ◊ anastomosis between descending aorta and pul. A. (Pott's operation).

b- ***Total correction:***

Complete restoration of the normal anatomy (open heart major surgery which is better done after the age of 2 years).

N.B.

- 1- **Fallot triology:** (→ ASD, Rt. vent. hypertrophy and Pulmonary stenosis).
- 2- **Fallot pentalogy:** (→ TOF and ASD)

B- OTHER CYANOTIC CHD WITH ↓ PUL. BLOOD FLOW

- ♦ The same general characters.
- ♦ Indistinguishable from TOF easily.
- ♦ The same lines of treatment as TOF.

	Pulmonary atresia with VSD	Pulmonary atresia without VSD	Tricusped atresia	Ebstein Anomaly
Antaomical Defect:	 • Atretic pulmonary valve • VSD • ± PDA	 • Atretic pulmonary valve • PFO • ± PDA	 • Atretic tricusped valve • PFO + VSD • ± PDA	 • Downward displacement of the tricusped valve leaflet ⇒ Huge Rt. At. ⇒ Small Rt. vent. ⇒ Tricusped reg.
Haemodyn-amics	• Blood in the Rt. ventricle passes only to VSD → Lt. vent. (mixed blood) → cyanosis • Pulmonary circulation is maintained through PDA or collaterals between aorta and pulmonary.	• Blood from Rt. side will pass through the only way (PFO) → cyanosis • Pulmonary circulation is maintained through PDA or collaterals between aorta and pulmonary	• Blood in Rt. atrium → PFO → Lt. atrium (Mixed blood) → Lt. ventricle then 1- VSD → Rt. vent. → Pul. A 2- Aorta (Mixed blood) → cyanosis	• It may persist silent for years but if huge Rt. atrial blood may pass through (PFO) from Rt to Lt. (cyanosis). • Tricusped regurge is a common finding.
Differences from TOF:	• Early and severe cyanosis • No specific murmur.	• Early and severe cyanosis. • No murmur • Death in neonatal period (when PDA closed) is common	• Early and severe cyanosis. • No specific murmur	• Asymptomatic. • If symptomatic. - Mild cyanosis - Arrhythmia - Picture of tricuspid regurge.

*** Cyanotic congenital HD with ↑ pul. blood flow ***

- This group is chch by:
 - ◆ Common attacks of heart failure.
 - ◆ Accentuated 2nd heart sound (↑S2).
 - ◆ Lung plethora in X-ray chest.
- The commonest example for this group is TGA:

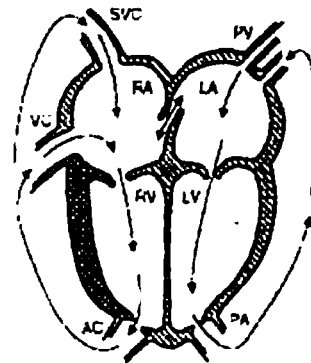
A- TRANSPOSITION OF GREAT ARTERIES

Anatomical defect:

- Aorta arises from Rt. ventricle while pulmonary artery arises from Lt. ventricle.
- There is usually a shunt to allow mixing of blood (PFO or VSD).
- PDA is essential → if closed death may occur.

Haemodynamics:

- Transposition results in supplying the tissues with unoxygenated blood → cyanosis.
- TGA results in (2) separate circulation which cannot maintain life except through PFO, VSD and PDA.
- Closure of PDA after birth → severe cyanosis.
- TGA may be isolated, with VSD, with VSD and PS or corrected TGA.



Clinical picture:

- Early cyanosis ± clubbing.
- Repeated H.F. and respiratory infection.
- Rare cyanotic spells.
- S2 accentuated but no significant murmur (except in large shunt).

Complications:

The same as TOF but recurrent chest infection instead of pulmonary TB.

Investigations:

- 1- Blood: Polycythaemia.
- 2- X-ray chest:
 - Lung plethora (except if TGA is associated with PS).
 - Usually Rt. vent. ++
 - Cardiac → Egg on side appearance.
- 3- ECG: ± Rt. vent. ++
- 4- ECHO: Diagnostic
- 5- Catheterization:
 - ⇒ O₂ saturation → ↑↑ in pulmonary artery.
 - ⇒ Pressure → ↑↑ in Rt. ventricle.

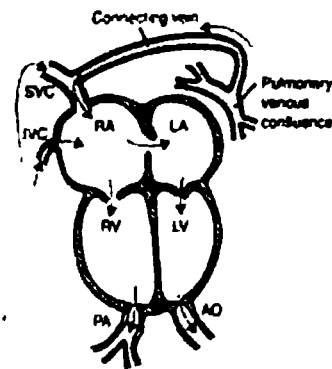
Treatment:

- 1- Palliative treatment ♦ PGE1 infusion (Maintain PDA)
 - ♦ Balloon atrial septostomy (Rashkind operation).
- 2- Surgical correction: ♦ Arterial switch (Jatene operation) aorta is connected to PA & PA is connected to aorta → anatomical
 - ♦ Atrial switch (Mustard operation) (by diverting blood from left atrium to right ventricle & from right atrium to left ventricle)

B- OTHER CYANOTIC CHD WITH ↑ PUL. BLOOD FLOW

☆ Total anomalies pulmonary venous return

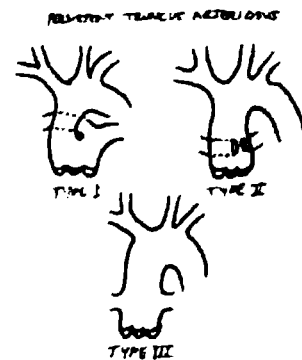
- ✧ The pulmonary veins open into the Rt. side of heart, either:
 - ♦ Supracardiac (in SVC)
 - ♦ Cardiac (in coronary sinus).
 - ♦ Infracardiac (in IVC or portal vein).
- ✧ ASD is usually present to allow the blood from pulmonary veins to reach the Lt. side (But infact mixed blood will reach the Lt. side) → cyanosis.
- ✧ Characteristic X-ray picture.
- ♦ Cardiac shadow → snowman (or) figure of (8) appearance.



☆ Truncus arteriosus

● Defect.

- ♦ One vessel (arterial trunk) leaves the heart and gives rise to both the aorta and the pulmonary.
- ♦ VSD usually present.
- ♦ Types of persistent truncus arteriosus:
 - Type I → single pul. artery from Lt. side.
 - Type II → 2 pul. arteries from post. wall.
 - Type III → 2 pul. arteries from lat. wall
 - Type IV → No pulmonary artery.



● Manifestations:

- Mixed blood is pumped through both aorta and pulmonary.
- Onset of cyanosis is variable.
- General manifestations of cyanotic CHD with ↑ pul. bl. flow

● Treatment: Urgent surgical correction in infancy.

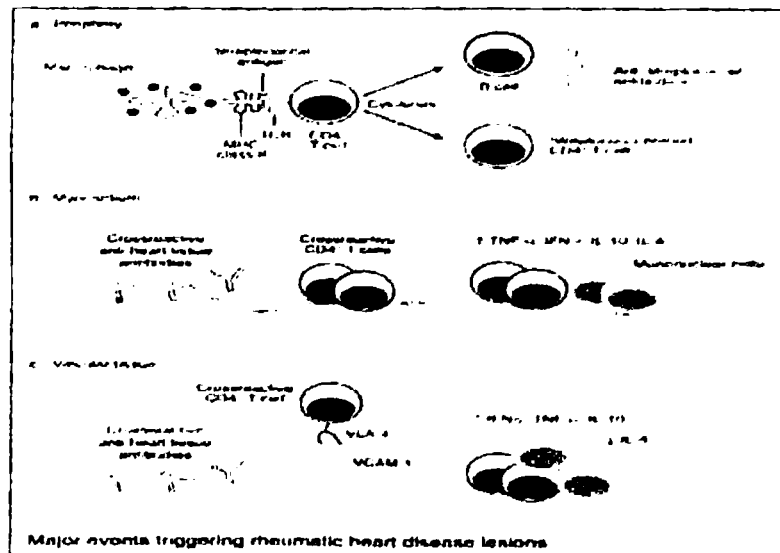
☆ Single ventricle

- ✧ Absence of interventricular septum. So both atria empty their blood into the common ventricle → blood is pushed in both pulmonary and aorta (mixed blood) → cyanosis.
- ✧ If associated with pulmonary stenosis → ↓ pul. bl. flow.



Pathogenesis:

2- Cross reaction: This strain possesses an antigen immunologically similar to that in heart connective tissue. So produced antibodies against streptococci, can react with the heart.



1-The incidence of acute rheumatic fever varies with geographic location and the population studied but, in general, ranges from 3 to 61 per 100,000 school children. The highest incidence occurs in children aged 5 to 15 years. This condition is rare in children younger than 4 years but does occur. Acute rheumatic fever is most common during winter and spring, a seasonal variation similar to that of streptococcal pharyngitis

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Diagnosis Of Rheumatic Fever:***Modified Jones criteria*****Major manifestations**

- Carditis
- Polyarthritis
- Chorea
- Subcutaneous nodules
- Erythema marginatum

Minor manifestations

- Arthralgia
- Fever
- Prolonged PR interval
- Elevated ESR ,↑ C reactive protein and Leukocytosis
- Prior rheumatic fever

The revised Jones criteria are used for the diagnosis of acute rheumatic fever , diagnosis is highly probable when either *two major manifestations* or *one major and two minor manifestations*, plus evidence of antecedent streptococcal infection, are present. The absence of supporting evidence of a previous group A streptococcal infection makes the diagnosis doubtful

NB :1-Two major manifestations are always stronger than one major +two minor

2-Arthralgia or prolonged PR interval cannot be used as a minor manifestation when using arthritis and carditis, respectively, as a major manifestation

Major criteria of Rheumatic fever:**1- Arthritis (75%)**

- ◊ Polyarthritis (> 3 joints)
- ◊ Big joints are affected (e.g. knee, wrist, elbow,).
- ◊ Fleeting: Migrating from one joint to the other.
- ◊ The affected joint shows: redness, hotness, swelling, limitation of movements ± effusion.
- ◊ Good response to salicylates.
- ◊ Spontaneous remission (in about one week) without residual deformity.

2- Carditis (50%)

All layer of the heart may be involved (Pancarditis):

❖ **Pericarditis:**

* Dry →

- Symptoms → Stitchy chest pain.
- Signs → Pericardial rub auscultated on the bare area or the apex in the form of superficial gritty to and fro sound not related to respiration (D.D. from pleural rub)

* Pericardial effusion → Uncommon,

- Symptoms → Dull aching pain
- Signs → ↑ cardiac dullness (dullness outside the apex & ↑ dullness of the bare area) with distant heart sounds on auscultation.

❖ **Myocarditis:**

- Disproportionate tachycardia (for age and fever).
- Gallop rhythm & muffled heart sounds.
- Prolonged P-R interval in ECG.
- In severe cases H.F. and arrhythmias may occur.

❖ **Endocarditis:** Mitral valve is commonly involved then Aortic (Tricuspid 5%)* **Mitral valve:**

- 1- Inflammatory oedema of the cusps during acute phase → transient mitral stenosis (Cary coomb's murmur).
- 2- Destruction and fibrosis of the mitral valve may occur → MR (persistent).
- 3- Organic mitral stenosis due to healing and adhesion of the cusps is late.

* **Aortic valve:**

Aortic regurge may occur but stenosis is usually late sequelae.

N.B.

- More than one valve (i.e. both aortic and mitral) and double lesions (stenosis and regurge in the same valve) are common.
- The cardiac damage ↑ by repeating attacks which may represent by new murmurs or accentuation of previously noticed murmurs.

3- Rheumatic chorea (10%)

"Sydenham's chorea"

- ◇ More common in girls > 8 years due to affection of the basal ganglia, usually self limited within 1-2 months (complete resolution)
- ◇ Occurs after weeks or months of strept. infection so other criteria and investigations of Rh. activity are usually absent.
- ◇ **Manifestations:**
 - I- **Involuntary movements:** Sudden involuntary jerky movements of
 - * The limbs (Fall of objects from the hand and unsteady gait)
 - * The tongue (Interrupted speech).
 - * The face (Abnormal movements).
 - II- **Hypotonia and hyporeflexia**
 - * Inability to keep the arm protruded but wrist flexion and finger hyperextension occurs (dinner fork appearance).
 - * Inability to keep the tongue protruded.
 - * Hypotonia may be severe enough to cause paralysis (chorea molis).
 - III- **Emotional instability:** (sudden laughing or crying).

4- Erythema marginatum (< 5 %)

- ◇ Wavy rings of erythema with sharp margins not itchy nor painful.
- ◇ Most common site is the trunk and proximal part of the extremities.
- ◇ Heat applying to the skin can accentuate the appearance of erythema marginatum.

5- Subcutaneous nodules (1 %)

- ◇ Firm, painless, mobile nodules under the skin.
- ◇ Mainly over the extensor surfaces and bony prominences e.g. scapula, elbow & chin of the tibia.
- ◇ It is usually associated with severe carditis.

Supporting evidence for antecedent Group A streptococcal infection

- ◆ Recent scarlet fever
- ◆ Positive throat culture
- ◆ Rapid streptococcal antigen test
- ◆ Elevated or rising streptococcal antibody titer – ASO[anti-streptolysin] - Anti DNaseB(antideoxyribonuclease B), AH[anti-hyaluronic acid]) .If these antibodies (>300 in children >200 in adults) suggest previous infection

DD Of Rheumatic Fever

- ◆ Juvenile rheumatoid arthritis
- ◆ Acute transient synovitis
- ◆ Viral myocarditis
- ◆ Bacterial arthritis
- ◆ Sick cell anemia
- ◆ Periarteritis nodosa
- ◆ Kawasaki disease
- ◆ Lupus erythematosus
- ◆ Dermatomyositis
- ◆ Henoch-Schonlein purpura
- ◆ Lyme disease
- ◆ leukemia

Prevention:

There are three aspects to the prevention of acute rheumatic fever

- (i) Prevention of acute rheumatic fever by accurate and prompt recognition and treatment of streptococcal pharyngitis
- (ii) prevention of recurrent acute rheumatic fever through compulsive ongoing prophylaxis against streptococcal infection
- (iii) prevention of bacterial endocarditis in individuals with chronic rheumatic cardiac valve disease.

Prophylaxis should be begun during the initial episode of rheumatic fever. Parenteral administration of 600,000 to 1.2 million U of benzathine penicillin G every 4 weeks is the most effective prophylactic regimen. Patients who have a history of allergy to penicillin can receive erythromycin, oral penicillin V (250 mg by mouth twice a day), oral sulfadiazine 1g or sulfisoxazole 0.5g once daily.

The duration of prophylaxis against rheumatic fever is controversial, but the following guidelines may be helpful.

- 1- Patients who had rheumatic fever without carditis should receive prophylaxis for 5 years or up to 21 years, whichever is longer.
- 2- Patients who had rheumatic fever with healed carditis but no valvular disease should receive prophylaxis for 10 years or into adulthood, whichever is longer.
- 3- Patients with residual carditis (persistent valvular disease) should receive prophylaxis until at least 40 years of age, for at least 10 years after the last episode, or perhaps for life

Treatment

When acute rheumatic fever is suggested by history and physical examination, one should obtain the following laboratory studies: complete blood count, acute phase reactants (erythrocyte sedimentation rate and C-reactive protein), throat culture, ASO titer (and a second antibody titer, particularly with chorea), chest x-ray films, and ECG. Cardiology consultation is indicated to clarify whether there is cardiac involvement; two-dimensional echo and Doppler studies are usually performed at that time.

- i- Bed rest: * For 2 weeks if there is no carditis.
 * For 4-6 weeks if there is carditis.

- ii- Diet: Light, nutritious, low salt diet.

iii- Eradication of streptococcal infection:

- * Procaine penicillin (I.M once daily) → dose 600,000 U/day for 10 days or
- * Penicillin V (oral/ 6 hours) → dose 50-100,000 U/Kg/day for 10 days. or
- * Erythromycin in penicillin allergy (oral/6 hrs) → dose 50 mg/k/d for 10 days.

iv- Anti-inflammatory drugs:

Salicylates: →

- * Indications → • Rheumatic fever without carditis.
 • If steroids are contra-indicated.
 • During steroid withdrawal.
- * Dose → • 100 mg/k/day (maximum 6 grams) for 2 weeks,
 then 75 mg/k/day (for another 4-6 weeks).
- * S.E. → • Bleeding
 • Gastric upsets
 • Rye syndrome.

Corticosteroids: →

- * Indications → • Presence of carditis (especially with cardiomegaly or HF).
- * Dose → • Prednisone 2mg/kg/day (maximum 60 mg) for 2 weeks
 followed by gradual tapering over 2-4 weeks.
- * S.E. → See later (especially prolonged course without tapering).

v- Other lines of ttt:

- * Rheumatic chorea → Haloperidol (Safinase tab.) 0.05 mg/k/day or chlorpromazine 0.5 mg/k/day.
- * Treatment of heart failure and infective endocarditis.
- * Surgical management of residual valvular lesions (Rheumatic heart disease).

VALVULAR DISEASES

Mitral Stenosis

○ Aetiology:

- 1- Rheumatic: Most cases.
- 2- Congenital: Very rare.

○ Haemodynamics:

- 1- Grade 1 → "Left atrial dilatation"
due to blood collection in it.

- 2- Grade 2 → "Congestive M.S."
due to blood accumulation in pulmonary veins
and capillaries → pulmonary congestion.

(Congestive pulmonary manifestations)

- 3- Grade 3 → "Hypertensive M.S."

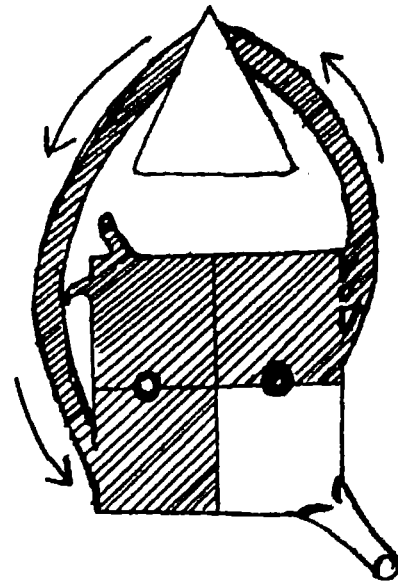
By time ↑↑ pulmonary vascular resistance occurs 2ry
to persistent pulmonary congestion → pulmonary
hypertension.

(Low COP manifestations)

- 4- Grade 4 → "M.S. with Rt. vent. failure"

Pulmonary hypertension → pressure overload on Rt. vent. → Rt. vent.
hypertrophy → By time Rt. vent. failure occurs.

(Congestive systemic manifestations)



○ Manifestations:

- 1- May be asymptomatic, discovered accidentally.
- 2- Congestive pul. → ↓ COP → Congestive systemic manifestations
- 3- Complications of M.S.:

❖ Mitral valve: SBE, Rh.activity, calcification.

❖ Lt. atrium: • Compression manifestations • Arrhythmias (A.F.)
• Lt. atrial thrombi → ± Embolization.

❖ Lungs: • Pulmonary infection. • Pulmonary infarction.

❖ Rt. Vent.: Right sided H.F.

○ Cardiac examination:

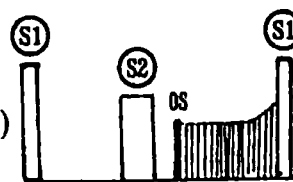
★ Insp., palp. and percussion:

- 1- Lt. atrium and Rt. vent. ++
- 2- Slapping apex.
- 3- Diastolic thrill on the apex.

• **Auscultation:**

1- **Heart sounds:**

- Accentuated S1.
- Opening snap: (just after S2 and before the murmur) due to opening of the thickened mitral valve.



2- **Murmur:**

- Mid diastolic rumbling with presystolic accentuation.
- Maximum intensity on the apex.
- Not propagated.

• If pulmonary hypertension develops special data of pul. hypertension will appear.

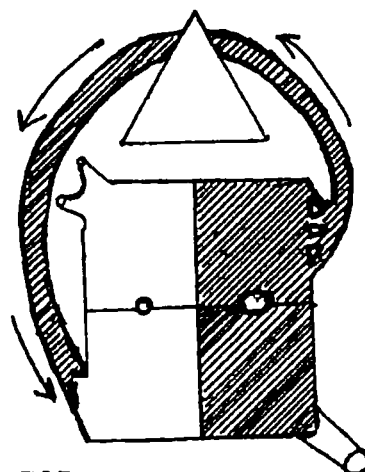
Mitral Regurge

○ **Aetiology:**

- 1- Rheumatic (Common). 2- Congenital (Rare) 3- Mitral valve prolapse

○ **Haemodynamics and manifestations:**

- 1- (May be asymptomatic early)
- 2- During Lt. vent. contraction some blood returned back to Lt. atrium through the incompetent mitral valve.
- 3- During diastole the large amount of blood in Lt. atrium will be pushed again to the left ventricle:
 - ↑ blood flow through mitral → (Relative M.S.)
 - Lt. ventricular dilatation.
- 4- Lt. vent. dil. → LVF → Pul. Congestion.



(Congestive pulmonary manifestations)

- 5- Prolonged pul. congestion → pul. hypertension → ↓ COP

(↓ COP manifestations)

- 6- Rt. sided failure is a very late event (± end stage)

(Congestive systemic manifestations) ⇒ uncommon

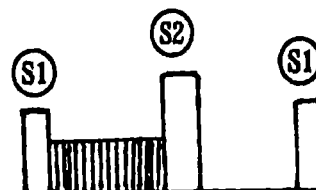
○ **Cardiac examination:**

• **Inspection, palpation and percussion:**

- Lt. ventricular ++
- Hyperdynamic apex.
- Systolic thrill on the apex.

• **Auscultation:**

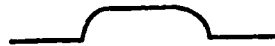
- Muffled S1.
- Pansystolic murmur on the apex propagated to the axilla (± Diastolic murmur of relative M.S.).



• **If pul. hypertension:** → see later

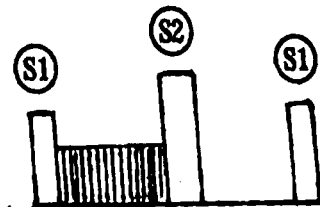
1- <u>Valvular A.S.</u> :	• Rheumatic	• Congenital
2- <u>Subvalvular A.S.</u> :	• Congenital	• Acquired (Post operative)
3- <u>Supravalvular A.S.</u> :	• Associated with William's syndrome.	

- 1- Obstruction of Lt. vent. outflow → (↓COP)
- 2- Lt. vent. overload → Lt. vent. ++
- 3- By time LV ++ → LV failure → (Congestive pulmonary)
- 4- General manifestation:
 - Small pulse volume (plateau pulse)
 - Narrow pulse pressure = ↓ (systole - diastole).



- Lt. ventricular ++
- Heaving apex.
- Systolic thrill on the base and neck.

- ♦ S2 show narrow splitting but normal or ↓ intensity.
- ♦ Ejection systolic murmur, harsh, loud on the 1st Aortic area, propagated all over the pericordium.
- ♦ Ejection click may precede the murmur in valvular A.S.



- 1-Ballon valvuloplasty:
When symptoms on exercise/ high resting pressure gradient(>64mmHg)
- 2-High risk of significant valvular insufficiency
- 3-Surgical valve replacement
- 4-Subacute bacterial endocarditis prophylaxis .

Aortic Regurg

○ Aetiology:

1- Rheumatic (Commonest) 2- Others (\$, Marfan syndrome, post operative in A.S.)

○ Haemodynamics and manifestations:

- 1- During diastole blood return from aorta to Lt. vent. → ↓ diastolic blood pressure.
- 2- L.V. receives blood from both Aorta and Lt. atrium so → ↑ systolic blood pressure.
- 3- By time ↑ Load on Lt. vent. → Lt. vent. ++ → Lt. vent. failure → congestive pulmonary symptoms → pul. hypertension → ↓ COP symptoms (late).
- 4- From (1) and (2) ↓ diastolic blood pressure and ↑ systolic blood pressure will lead to peripheral signs of Aortic regurge which are:

- **Corrigan sign** → Marked carotid A. pulsations.
- **De-Musset sign** → Nodding of the head.
- **Thrill** over the carotid area (systolic).
- **Water-hammer pulse.**
- **Capillary pulsations** in nails (± lips, ear, ...)
- **Blood pressure** shows (↑ systole and ↓ diastole).
- **Pistol shot:** Loud sound heard over the femoral artery (or any large artery) by the stethoscope.
- **Durozeir sign:** Double murmurs are heard on femoral A. (by stethoscope).
- **Hill's sign:** Blood pressure in LL > UL by 20-40 mmHg (Normally BP in LL > UL by 10-15 mmHg).



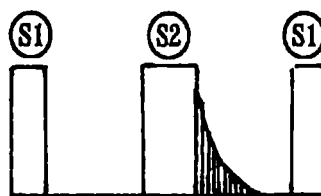
○ Cardiac examination:

✱ Inspection, palpation and percussion:

-
- Lt. ventr. ++
 - Hyperdynamic apex.

✱ Auscultation:

- ♦ S2 → weak
- ♦ Early diastolic murmur on 2nd Aortic area ± propagated to the apex (Better heard in end of expiration).



Pulmonary Stenosis

○ Aetiology:

- Congenital
- Acquired (Rare)
- May be: valvular, subvalvular or supra-valvular.

○ Haemodynamics and manifestations:

- Obstruction to Rt. ventricular outflow → Rt. vent. overload → Rt. vent. ++ → Rt. vent. failure → congestive systemic symptoms.
- Due to obstruction → ↓ Pul. flow → ↓ pul. veins filling → ↓ Left side flow → ↓ COP manifestations.

○ Cardiac examination:

• Insp., palp. and perc.:

- Rt. vent. ++
- Systolic thrill on pulmonary area.

• Auscultation:

- Muffled S2.
- Ejection systolic murmur maximum over pulmonary area may propagate to the pericardium.

○ Treatment:

- **Mild:** (peak systolic gradient < 50 mmHg)
 - ♦ Treatment not indicated
 - ♦ SBE prophylaxis
- **Moderate-severe** (>50 mmHg)
 - ♦ Transcatheter balloon valvuloplasty
- **Neonatal critical PS**
 - ♦ Character: cyanosis and RV dysfunction
 - ♦ Temporary stabilization with IV prostaglandin E infusion
 - ♦ Early transcatheter balloon valvuloplasty

Pulmonary Regurg

- Rarely congenital most probably 2ry to pulmonary hypertension or post operative.
- Rt. Vent. ++ and systemic congestion are common.
- Early diastolic murmur on pulmonary area.

Tricuspid Stenosis

- Usually functional (Any cause which ↑ flow through the valve), very rarely organic.
- Systemic congestion and ↓ COP.
- Murmur (Mid-diastolic rumbling) at the left lower sternal angle (+ Accentuated S1).

Tricuspid Regurge

- Usually due to Rt. vent. ++ or 2ry to pulmonary hypertension.
- Systemic congestion and Rt. sided heart failure.
- Pan systolic murmur on left lower sternal angle and may propagate to the apex (+ Muffled S1).

Pulmonary Hypertension

- ✧ ↑↑ Pulmonary artery pressure above 30/15 mmHg.
- Inspection → Pulsations on the pulmonary area.
- Palpation → Diastolic shock on the pulmonary area (Palpable S2).
- Percussion → Dullness on the pulmonary area.
- Auscultation → • Accentuated S2
 - Ejection systolic murmur on pulmonary area $\pm$ systolic thrill

□ INFECTIVE ENDOCARDITIS □

✿ **Def.** Infective endocarditis is an infection that affects some part of the endocardium. The infection usually involves one or more heart valves which are part of the endocardium

✿ How does infective endocarditis occur and progress?

Most cases are caused by infection with bacteria. A small number of cases are caused by infection with fungi. The blood usually does not contain any bacteria or fungi. However, some may get into the blood if you have an infection or wound in another part of the body. In particular, dental and mouth infections are situations where bacteria can quite easily get into the bloodstream.

Most bacteria that get into the bloodstream are killed by the immune system. However, sometimes some bacteria survive and settle on a heart valve (particularly if the valve is already damaged in some way), or on another section of the endocardium. Once a small focus of infection develops in the endocardium it is difficult for the immune system to clear it

In time, small clumps of material called vegetations may develop on infected valves. The vegetations contain bacteria or fungi, small blood clots, and other debris from the infection. The vegetations may prevent affected valves from opening and closing properly. The infection can also damage affected valves, and may spread to other areas of the endocardium or heart tissue. Fragments of the vegetations may also break off and travel in the bloodstream to other parts of the body.

There are differences in the different clinical situations:

Acute IE:

The thrombus may be produced either by the invading organism or by valvular trauma (pacing wires, catheters, etc.).

Subacute IE:

Sufficient inoculum of bacteria required to allow invasion of the thrombus, bacteria clumping with production of agglutinating antibodies.

Nonbacterial thrombotic endocarditis:

This can result from, for example, renal failure, neoplasia, systemic lupus erythematosus (SLE) or malnutrition.

The valves most commonly affected by infective endocarditis are (in decreasing order of frequency):

- Mitral valve
- Aortic valve
- Combined mitral and aortic valve
- Tricuspid valve
- Pulmonary valve - rare

The organisms responsible for infective endocarditis

- ***Staphylococcus aureus*:**
The most common cause of IE overall (acute and subacute); most common with prosthetic valves, acute IE, and IE related to intravenous drug abuse. High mortality rate.
- **Coagulase negative *S. aureus*:**
- causes subacute disease similar to *Streptococcus viridans*. Accounts for 30% of IE associated with prosthetic valves.
- ***S. viridans*:**
50-60% of subacute IE cases.
- **Group D streptococci:**
Usually subacute and the third most common cause of IE.
- **Group A, B, C and G streptococci:**
- ***Pseudomonas aeruginosa***
Usually acute IE and requires surgery for cure.
- **HACEK organisms (*Haemophilus aphrophilus*, *Actinobacillus actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens*, *Kingella kingae*):**
Usually subacute disease and about 5% of all IE.
- **Fungi:**
Cause subacute disease.
- **Enterococci.**

*Presentation

- Early disease subtle and nonspecific
- Indolent process which may include:
 - Fatigue
 - Low-grade fever
 - Flu-like illness
 - Polymyalgia-like symptoms
 - Loss of appetite
 - Back pain
 - Pleuritic pain
 - Abdominal symptoms (may be pain, vomiting and appendicitis-like symptoms)
 - Weight loss
 - Cerebrovascular accident - less common
 - Congestive cardiac failure - less common
- May be history of risk factors.

-Developing disease produces further clinical features of embolic or immunological origin when treatment/diagnosis delayed for weeks/months:

- Acute meningitis - signs and symptoms but with sterile CSF
- Hemiplegia from emboli in the middle cerebral artery (50% of patients may be first manifestation; has high mortality)
- Splenic infarction causing pain
- Blindness from retinal artery occlusion
- Myocardial infarction from emboli in the coronary artery
- Pulmonary emboli
- Interstitial nephritis or proliferative glomerulonephritis from deposition of circulating immune complexes and may cause hematuria or renal failure.
- Renal failure may result
- Musculoskeletal symptoms (nearly half of patients) often from immunologically mediated synovitis
- Immune-mediated vasculitis (causing Osler's nodes and Roth's spots)
- Palpitations from immune-mediated myocarditis
- Back pain (15% of patients) may have origin in immune complex deposition in disc spaces

Examination

Fever: chronically ill patients (subacute IE) may not have fever, but the majority do

Heart murmurs:

- Most patients have a murmur
- Only 15% have the classic 'changing murmur'
- Most common murmur is aortic regurgitation

Petechiae:

- Conjunctivae
- Hands and feet (dorsum)
- Chest and abdominal wall
- Oral mucosae and soft palate

Splinter or subungual haemorrhages: Linear and red

Osler's nodes: small tender red-to-purple nodules pulp of terminal phalanges fingers and toes

Clubbing: only 10% of cases and usually in longstanding subacute IE

Roth's spots: retinal haemorrhages with pale centres

Janeway's lesions: irregular painless erythematous macules on the thenar and hypothenar eminence (usually with acute IE and *S. aureus*)

Arthritis:

- With subacute IE usually asymmetric and up to 3 joints affected .
- Acute IE can give acute septic monoarticular arthritis

Splenomegaly

Meningism/meningitis: purulent disease occurs in acute IE and aseptic variety in subacute IE

Differential diagnosis

- SLE
- Atrial myxoma and other cardiac neoplasms
- Lyme disease
- Antiphospholipid syndrome
- Polymyalgia rheumatica
- Reactive arthritis

Investigations***Blood cultures***

- Blood cultures are used to demonstrate bacteraemia of 30 minutes or more duration
- Draw 3 to 5 sets of blood cultures over 24 hours
- In acute IE, 3 sets drawn from different venepuncture sites over 30 minutes demonstrates continuous bacteraemia
- Blood should not be drawn from IV lines (unless diagnosing line infection when simultaneous line and peripheral vein sampling may be used)
- Prior use of antibiotics commonly gives false negative results
- Probably 50% of culture results are estimated to be falsely positive
- Fastidious organisms may require special culture media or prolonged incubation

Serological tests

- These may be necessary to detect some organisms, eg legionella, chlamydia, brucella and coxiella species.

Imaging studies

- Echocardiography is the indirect investigative method of choice. Echocardiography is especially of use when clinical picture of IE but negative cultures
- Echocardiography is useful to predict complications such as embolisation:

Diagnostic criteria

The Duke criteria - for definitive clinical diagnosis requires either 2 major or 1 major and 3 minor or 5 minor criteria from the list below:

Major blood culture criteria:

- 2 positive blood cultures for typical IE organisms
- Persistently positive cultures for such organisms drawn >12 hours apart
- 3 or more positive cultures drawn at least 1 hour apart

Major echocardiographic criteria:

- Positive result and no alternative explanation
- Myocardial abscess
- Partial dehiscence of prosthetic valve
- New valvular regurgitation

Minor criteria:

- Predisposing cardiac condition
- Fever (38°C or over)
- Elevated C-reactive protein or erythrocyte sedimentation rate
- Vascular lesions
- Immunological phenomenon
- Positive cultures less than 'major'
- Positive echocardiographic results but insufficient for major criteria

Complications

These are an inherent part of the progression of the disease. Patients should be monitored for:

- Valve dysfunction
- Myocardial abscesses
- Embolic phenomena
- Heart failure
- Metastatic infection
- Immunological disease and organ dysfunction
- Complications even after bacteriological cure
- Conduction defects (patients with IE should have daily ECGs)

Treatment for infective endocarditis***Antimicrobial therapy***

Strong antibiotic combination without waiting for the results of blood culture (But may be changed according to culture results).

Combination of the following drugs (I.V. for 4 weeks) is advisable.

- ✧ Penicillin G 200,000 U/K/day.
- ✧ Gentamycin 5-7 mg /K/day.
- ✧ Vancomycin 40-60 mg /K/day (Due to the high incidence of MRSA).

N.B: In fungal endocarditis liposomal amphotericin B or voriconazole may be used.

Surgery

✧ Antibiotic treatment is all that is required in many cases. However, an operation is needed in up to half of cases when the infection is more severe. An operation can be life-saving.

✧ Operations that may be done include:

- Replacing a damaged valve with an artificial valve.
- Valve repair if the damage is less severe and repair is possible.
- Drainage of any abscesses (collections of pus) that may develop in the heart muscle or in other parts of the body.

Can infective endocarditis be prevented?

1- Oral & dental care

2- Patients with risk factors who will be exposed to surgical procedures must receive prophylactic antibiotics as follow:

Procedure	1 hr before surgery	6 hr after surgery
Oral & dental	Oral amoxycillin (50 mg/kg)	Oral amoxycillin (25 mg/kg)
GIT & Genitourinary	Parental ampicillin (50 mg/kg) & gentamicin (2 mg/kg).	↓ same

≡N.B: Erythromycin, Clindamycin & Vancomycin are alternatives for cases already receiving long acting penicillin prophylaxis or penicillin sensitives

□ HEART FAILURE □

• Definition:

Congestive heart failure (CHF) occurs when the heart can't meet the metabolic demands of the body (failure of the heart to supply the tissue with their needs of blood)

• Aetiology:

I) Cardiac Causes :

- Congenital heart disease
- Acquired heart disease (rheumatic valvular HD as MR, AR)
- Myocardial dysfunction as Myocarditis
- Cardiac arrhythmia as SVT

II) Non cardiac:

- Hypertension, Anemia, sepsis
- Bronchopulmonary dysplasia in premature
- Acute cor pulmonale due to airway obstruction

Causes according to finding

1-Pressure over load

- Structural heart disease :
- Congenital heart diseases : as aortic stenosis (AS) and coarctation of aorta (CoA)
- Systemic hypertension

2-Volume over load

- Structural heart disease :
- Congenital heart diseases: V.S.D., P.D.A.
- Acquired heart diseases: rheumatic valvular HD (AR, MR)
- Anemia, sepsis

3-Myocardial dysfunction: it may be either

a- Systolic dysfunction or failure:

↓ ventricular contractility → ↓ c.o.p.

- Myocarditis
- Dilated cardiomyopathy
- Malnutrition

b- Diastolic dysfunction or failure:

↓ ventricular compliance, → ↑ venous pressure to maintain adequate filling.

- Hypertrophic cardiomyopathy
- Restrictive cardiomyopathy

Compensatory mechanisms

- Increasing the heart rate
- Hypertrophy of muscle
- Dilatation of heart
- Increasing the preload

As the demands on the heart exceed the normal range of physiologic compensatory mechanism signs of CHF occurs

Precipitating factors

1. Infection
2. Physical and emotional stress
3. Excessive salt intake
4. I.v. fluid or corticosteroid therapy
5. Severe anemia
6. Discontinuation of digitalis therapy
7. Arrhythmias

Clinical picture:***1-Tachycardia******2-Right-sided failure (systemic venous congestion)***

- Hepatomegaly
- Ascites
- Pleural effusion
- Edema
- Jugular venous distension

3.Left-sided failure(plumonary venous congestion)

- Tachypnea (dyspnea)
- Intercostals retractions
- Nasal flaring or grunting
- Rales (crepitations)
- Pulmonary edema

4.Low cardiac output

- Fatigue or low energy
- Pallor ,sweating
- Cold extremities
- Poor growth
- Dizziness
- Altered consciousness ,syncope

5.Left ventricular enlargement:

- Apex shifted outward and downward
- Localized apex

6.Right vehntricular enlargement:

- Apex shifted outward, and diffuse .
- Retraction of apex with simultaneous left parasternal space bulge (rocking)
- Parasternal and epigastric pulsation
- Dullness over the right half and lower part of the sternum
- Precordial bulge
- Functional murmur of tricuspid and mitral incompetence due to dilatation of heart

Uncompensated CHF**In an infant:**

- Failure to thrive
- Renal and hepatic failure

In older children:

- Low cardiac output manifestations
- Renal and hepatic failure

Investigations:**I) Laboratory testing includes:**

- Complete blood cell count (CBC) : anemia or infection
- Oxygen saturation
- Electrolyte levels :
 - hyponatremia due to water retention
 - elevated potassium level due to renal dysfunction or tissue destruction due to low cardiac output
- Blood gas abnormalities :
 - respiratory alkalosis in mild form of CHF
 - metabolic acidosis due to low cardiac output
 - lactic acidosis and decrease the serum bicarbonate level due to tissue hypoxia
- Renal and hepatic function due to decreased renal blood flow : increased urea and creatinine levels

II) Chest radiograph;

- Cardiomegaly is almost always present except in restrictive cardiomyopathy.
- Increased pulmonary blood flow

III) ECG: may show cardiomegaly or arrhythmia**IV) Echocardiography to identify potential cardiovascular causes.****V) Pulse oximetry**

Management of CHF

I) General measures

- Improving oxygen delivery: Administration of oxygen (40-50%) with humidity.
- Sedation :
 - Morphine sulfate 0.1-0.2mg/kg/dose/4hs s.c.
 - Phenobarbitone 2-3 mg /kg /dose /8hs oral or i.m.
- Salt restriction:
 - low salt formula in infants,
 - In older children :less than 0.5g/day and avoidance of salt.
- Daily weight measurement
- Treatment of the cause as hypertension
- Elimination and correction of predisposing factors as anemia, infection.
- Nutrition : CHF increases the metabolic demands while making feeding itself more difficult.

II) Drug therapy

A- preload reduction by diuretics:

- loop diuretic as
 - Furosemide 1 mg/kg/dose IV, 2 -3mg/kg/d PO / bid or tid
 - Ethacrynic acid 1 mg/kg/dose IV, 2 -3mg/kg/d PO / bid or tid.
- Thiazides diuretic as Hydrochlorothiazide 20 - 40 mg / kg /d / PO /bid or tid
- Aldosterone antagonists as spironolactone 2 -3mg/kg/d PO /bid or tid.

Side effect of diuretic therapy

I- hypokalemia

II- hypochloremic alkalosis

both may increase digitalis toxicity.

B-Rapidly acting inotropic agents : Enhancing cardiac contractility

Indication :

- 1-Critical ill infants with CHF
- 2- Those with renal dysfunction as COA
- 3-Postoperative cardiac patients with CHF

I- Dopamine 5-10 mcg/kg/min IV,

II-Dobutamine 5-8 mcg/kg/min IV.

Side effects : tachycardia, arrhythmias, hypertension or hypotension

C -Digitalis glycoside (digoxin)

Age	Tdd $\mu\text{g/kg}$	Maintenance $\mu\text{g/kg/day}$
Premature	20	5
Newborn	30	8
Under 2ys	40-50	10-12
Over 2ys	30-40	8-10

Method of digitalization base line ECG and serum electrolytes.

Tdd is divided into 3 doses:

1/2 dose.....initially

1/4 dose.....after 8hs

1/4 dose.....after another 8hs

Maintenance dose is divided into 2 equal doses every 12 hs after 12 hours from the last dose of TDD.

obtain ECG :

- before final Tdd,
- at start maintenance
- when suspect digitalis toxicity.

Important signs of toxicity are: vomiting and arrhythmias

Serum level is indicated if:

- Unsatisfactory therapeutic response
- Digitalis toxicity is suspected

N.B. During therapy calcium, atropine, hypokalemia should be avoided

Treatment of digitalis toxicity:

- ◆ Stop the drug
- ◆ Atropine 0.01 mg/kg/dose/iv...maybe repeated
- ◆ Phytointin 3-5 mg/kg/dose/iv over 10 min...maybe repeated
- ◆ Correct hypokalemia if present

D- Afterload reduction is divided into

- ◆ Arteriolar vasodilators: hydralazine 1.5 $\mu\text{g/kg/min/IV}$.
- ◆ Venodilators: nitroglycerin (their use is rare in common practice)
- ◆ Mixed vasodilators:
 - 1-Angiotensin-converting enzyme (ACE) inhibitors:
 - Captopril : 0.1-0.5 mg/kg/d PO
 - Enalapril: 0.1 mg/kg/d PO
 - 2-Nitroprusside 0.5-8 $\mu\text{g/kg/min/IV}$

□ CARDIAC INVESTIGATIONS □

I -Chest Radiograph

- An essential cardiac evaluation
- What information gained from x-ray:
 - Heart size and silhouette
 - Enlargement of specific cardiac chambers
 - Pulmonary blood flow and vascular marking
 - Others:
 - Lung parenchyma, - Spine
 - Bony thorax - Abdominal situs

Views Of X-ray

- ❖ Postero-anterior view
- ❖ Antero-posterior view
- ❖ Lateral view
- ❖ RT anterior oblique
- ❖ LT anterior oblique

The Normal Chest Radiograph

Posteroanterior view

- *the right cardiac border : SVC & the right atrium
- *the left cardiac border: Aortic knob, main PA , LV

NB : The left atrial appendage rarely contributes to the left heart silhouette

Lateral view and left anterior oblique view

- *the anterior chamber is the right ventricle
- *the posterior chamber is the inflow tract of the left ventricle.
- * Increased convexity of the anterior cardiac chamber suggests right ventricular dilation

NB :The main advantage of this view is to evaluate right and left ventricular dilation

Right anterior oblique view

- *the anterior chamber is the right ventricle, and the convexity above it is the pulmonary artery
- *Posteriorly, the inferior shadow is right atrium, and above it lies the left atrium
- *The main advantage of this view is demonstration of left atrial enlargement

EVALUATE SKELETAL ASPECT

- Centralization of the Patient
- Pectus excavatum → cardiomegaly
- Scoliosis → shift of the mediastinum
- Rib notching → CoA

EVALUATE PULMONARY VASCULARITY:

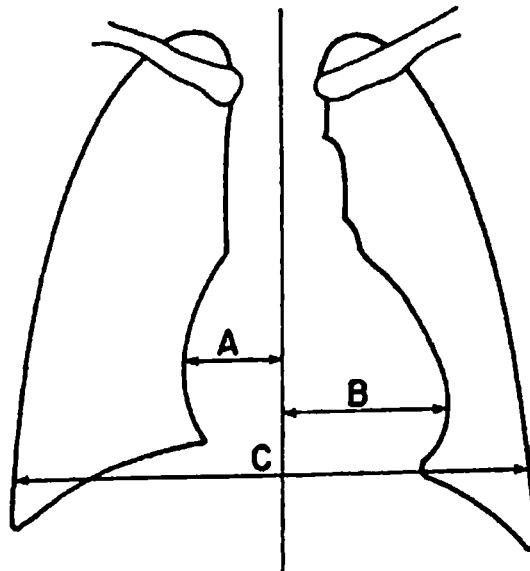
- Normal
- Decreased: lung oligemia
- Increased : lung plethora , pulmonary congestion

EVALUATE HEART

• **POSITION.** levocardia, dextrocardia, mesocardia

• **SIZE**

The CT ratio is obtained by dividing the largest horizontal diameter of the heart (A + B) by the longest internal diameter of the chest . The CT ratio In neonate > 60 % and > 50 % in infant meaning cardiomegaly.

▪ **SPECIFIC SHAPE**

*Boot shaped :Tetralogy of Fallot

*Egg on side : (TGA)

*Snowman or figure of 8(total anomaly pulmonary venous return ,supracardiac type)

*Flask heart (pericardial effusion)

• **Chamber enlargement**

***RT atrial enlargement:** this cause displacement of right cardiac border outward

***LT atrial enlargement**

1-enlargement of LAA causes straightening or convexity of the left cardiac border(mitralization)

2- The outline of the enlarged LA can be seen through the RA shadow (double contour)

3- barium swallow. The oesophagus displaced backwards by the enlarged LA.

***LV enlargement:**

Displacement of the apex downwards and outwards sometimes below the diaphragmatic shadow

***RV enlargements:**

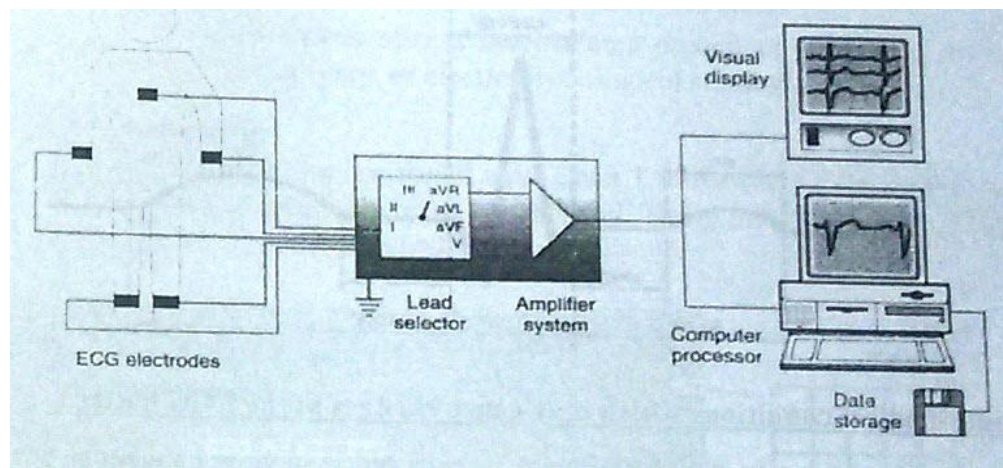
There are no reliable signs for diagnosis in the PA view, but better seen in the lateral view .However, it may displace the apex outwards which become separated from the diaphragm.

II-Electrocardiography

An ECG is one of the simplest and fastest procedures used to evaluate the heart.

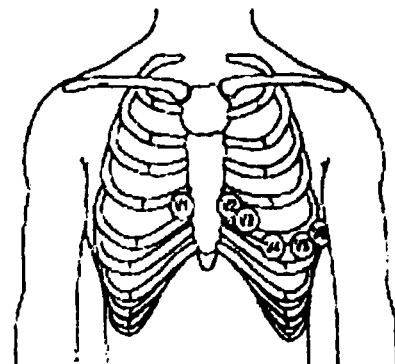
Components used in the recording and processing of an electrocardiogram

- Electrodes (small, plastic patches) are placed at certain locations on your child's chest, arms, and legs.
- When the electrodes are connected to the ECG machine by lead wires, the electrical activity of your child's heart is measured, interpreted, and printed out for the physician's information and further interpretation .



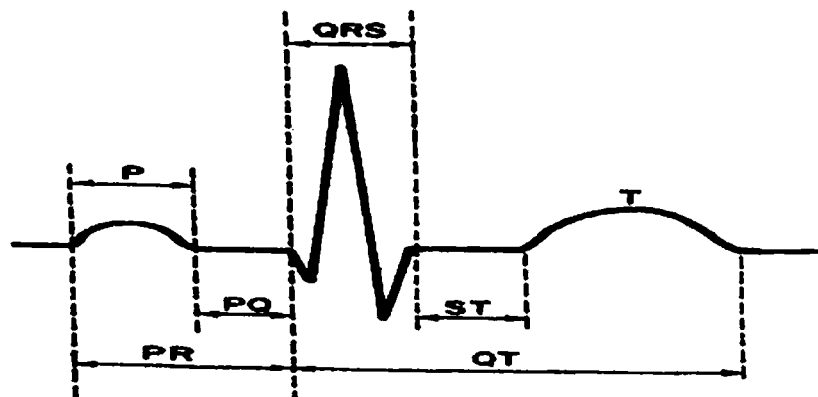
Position of the six chest electrodes for standard 12 lead electrocardiography:

- V1: right sternal edge, 4th intercostal space;
- V2: left sternal edge, 4th intercostal space;
- V3: between V2 and V4;
- V4: midclavicular line, 5th space;
- V5: anterior axillary line, horizontally in line with V4;
- V6: midaxillary line, horizontally in line with V4



What an ECG mean:

- The first little upward notch of the ECG tracing is called the "P wave." The P wave indicates that the atria
- The next part of the tracing is a short downward section connected to a tall upward section. This next part is called the "QRS complex."
- The next short flat segment is called the "ST segment." The ST segment indicates the amount of time from the end of the contraction of the ventricles to the beginning of the "T wave" before the ventricles begin to contract for the next beat .
- The next upward curve is called the T wave. The T wave indicates the recovery period of the ventricles

**Some medical conditions which may cause changes in the ECG pattern:**

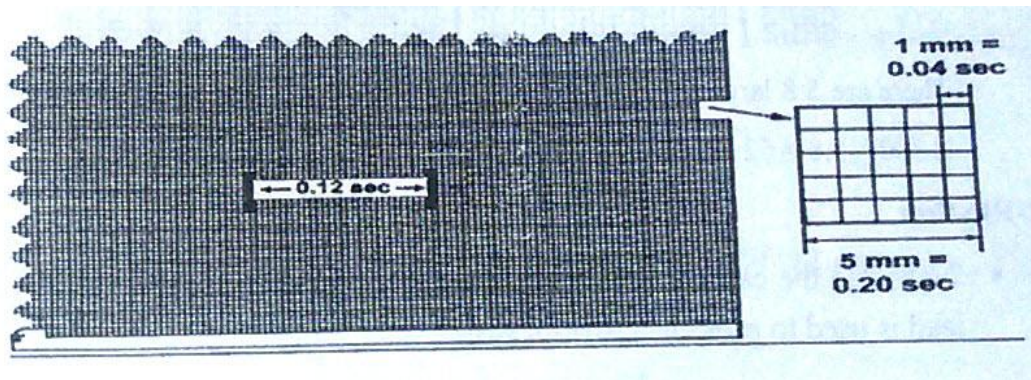
- Conditions in which the heart is enlarged such as congenital heart defects, valve disorders, high blood pressure, congestive heart failure.
- Ischemia - decreased blood flow to the heart muscle due to clogged or partially-clogged arteries .
- Conduction disorders - a dysfunction in the heart's electrical conduction system, which can make the heart beat too fast, too slow, or at an uneven rate .
- Electrolyte disturbances - an imbalance in the level of electrolytes, or chemicals, in the blood, such as potassium, magnesium, or calcium .
- Pericarditis - an inflammation or infection of the sac which surrounds the heart .
- Valve disease - malfunction of one or more of the heart valves may cause an obstruction of the blood flow within the heart .
- Chest trauma - blunt trauma to the chest, such as a motorist hitting the steering wheel in an automobile accident .

Indication for ECG:

- During a physical examination to obtain a baseline tracing of the heart's function (This baseline tracing may be used later as a comparison with future ECGs, to see if any changes have occurred)
- As part of a work-up prior to a procedure such as surgery to make sure no heart condition exists that might cause complications during or after the procedure
- To check the function of an implanted pacemaker
- To check the effectiveness of certain heart medications
- To check the heart's status after a heart-related procedure such as a cardiac catheterization, heart surgery, or electrophysiological studies

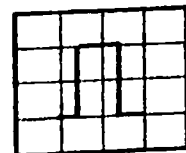
Electrocardiogram paper.

Time is measured on the horizontal axis. Each 1 mm equals 0.04 second, and each 5 mm (a large division) equals 0.20 second. Thirty millimeters (or six large divisions) equal 1.2 second or 1/50 minute

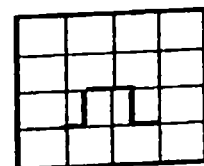


Standardisation of ECG

- ❖ A full standard means that the ECG was not reduced in size so as to fit on the paper. the rectangle's height is 2 big squares if it is full standard



- ❖ If the ECG is half standard, then the rectangle will be one large square high.

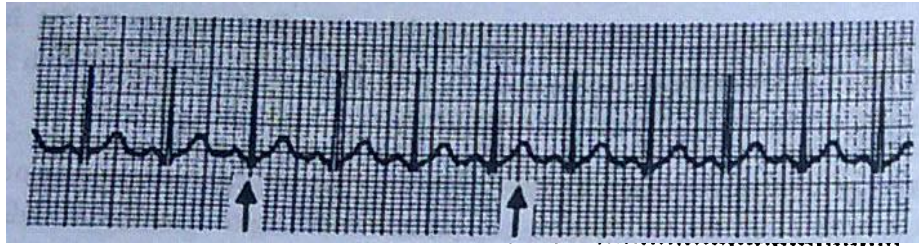


*****Important:** If the ECG is half standard you *MUST* multiply all waves by 2 to normalize them

Basic measurements for interpretation of an ECG

1-Heart rate:

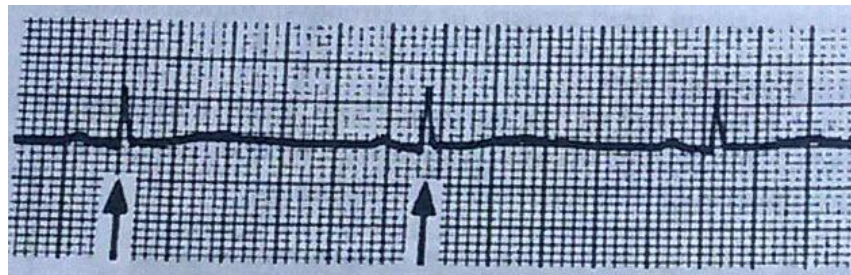
- Count the R-R cycle in six large divisions (1/50 minute) and multiply it by 50



There are about 3.3 cardiac cycles (R-R intervals) in six large divisions.

Therefore the heart rate is $3.3 \times 50 = 165$

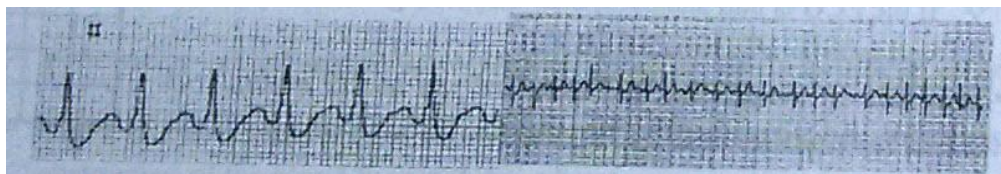
- When the heart rate is slow, count the number of large divisions between two R waves and divide that into 300 (because 1 minute = 300 large divisions)



There are 5.8 large divisions between the two arrows. Therefore, the heart rate is $300 \div 5.8 = 52$

2-Rhythm

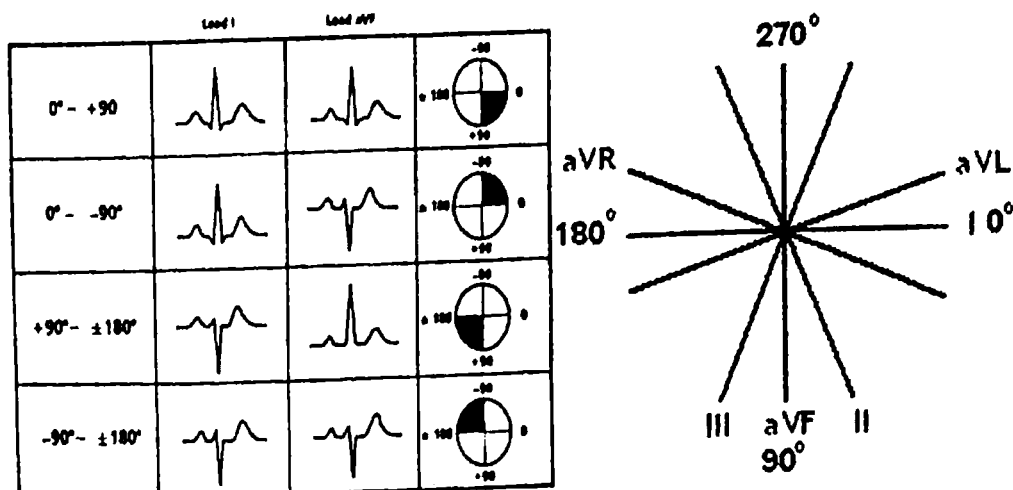
- To assess the cardiac rhythm accurately, a prolonged recording from one lead is used to provide a rhythm strip.
- Lead II, which usually gives a good view of the P wave, is most commonly used to record the rhythm strip.
- The term "sinus rhythm" is used when the rhythm originates in the sinus node and conducts to the ventricles.



Regular rhythm

An irregular rhythm.

3- QRS axis



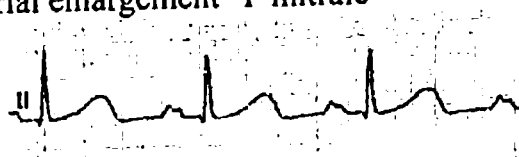
Locating quadrants of mean QRS axis from leads I and aVF

- Normal ranges of QRS axis vary with age.
- Newborns normally have RAD($+30$ to $+180$) compared with the adult standard.
- By 3 years of age, the QRS axis approaches the adult mean value of (-30 to $+105$)

4-P wave:

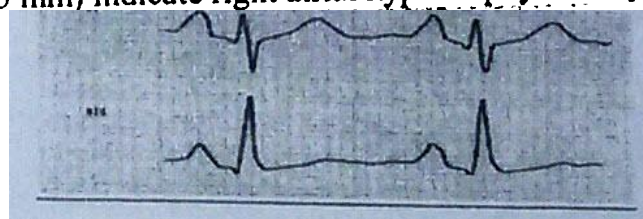
- Durations

P wave: Normally less than 2-3 small squares (0.08-0.12 sec) wide. Wide P waves indicate left atrial enlargement "P mitrale"



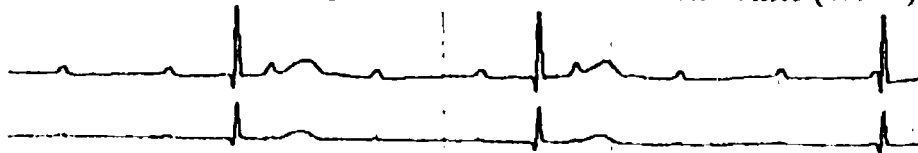
- Amplitude:

Tall P waves (>3 mm) indicate right atrial hypertrophy or "P pulmonale"



5-PR interval:

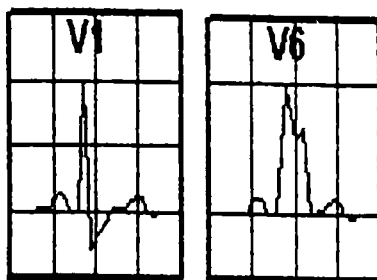
- The normal PR interval varies with age and heart rate (0.12 -0.16 sec)
- If longer than what is appropriate for age, that's first degree AV block .is seen in myocarditis, digitalis toxicity, certain congenital heart defects (ECD, ASD, Ebstein's anomaly), hyperkalemia
- A short PR interval is present in Wolff-Parkinson-White (WPW)

**6-QRS duration:**

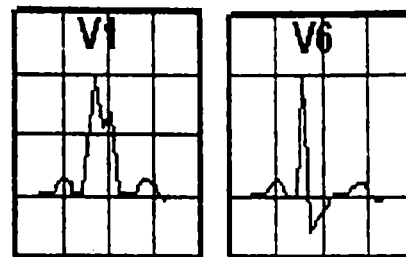
- If longer than 2-3 square (0.08-0.12 sec), that's bundle branch block (BBB).

RBBB or LBBB?

To determine if a block is right BBB versus left BBB, look for the "M" shaped QRS. If you see it in V1 (right chest lead) then it is RBBB, if you see it in V6 (left chest lead), then it is LBBB



LBBB

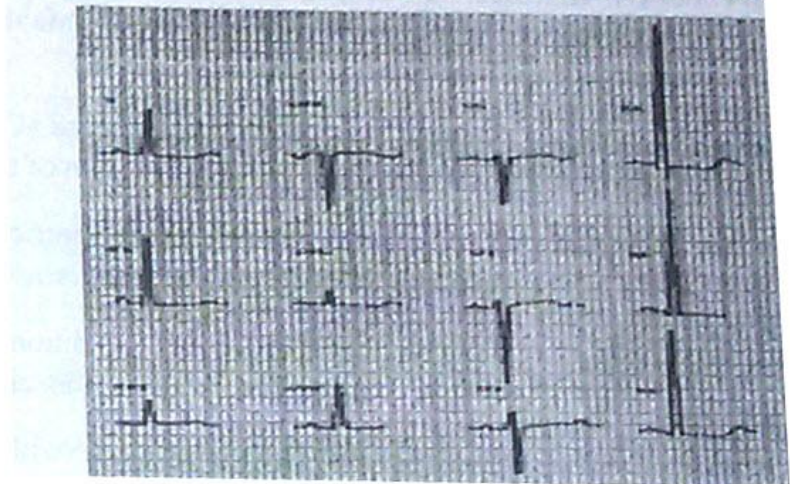


RBBB

7-QRS amplitude**Right ventricular
hypertrophy**

Dominant R wave in
leads V1, is sign of

**left ventricular
hypertrophy** . There
are tall voltages in
the left precordial
and limb leads



III-Echocardiography

A- M-MODE ECHOCARDIOGRAPHY

1. Measurement of the dimensions of cardiac chambers and vessels, thickness of the ventricular septum, and free walls
2. Left ventricular systolic function
3. Study of the motion of the cardiac valves (e.g., mitral valve prolapse, mitral stenosis, pulmonary hypertension) and the interventricular septum
4. Detection of pericardial fluid

B-TWO-DIMENSIONAL ECHOCARDIOGRAPHY

1. To screen routinely newborns and small infants who appear to have cardiac defects or dysfunction
2. To rule out cyanotic congenital heart disease (CHD) in newborns with clinical findings of persistent pulmonary hypertension of the newborn (PPHN .)
3. To diagnose PDA, other heart defects, or ventricular dysfunction in a premature infant who is on a ventilator for pulmonary disease

To rule in or rule out important cardiac conditions that are suspected on the basis of routine evaluation (e.g., cardiac examination, chest x-ray films, ECG.
4. To follow up on conditions that may change with time or treatment (e.g., before and after indomethacin treatment for PDA in premature infants, evaluation of drug therapy for CHF or LV dysfunction, follow-up examination for certain congenital or acquired heart diseases
5. Before cardiac catheterization and angiocardiography, to obtain certain information that can reduce the amount of time spent in the cardiac catheterization laboratory and the amount of the radiopaque dye injected and to gain some information that angiography cannot provide.
6. To replace cardiac catheterization and angiography in certain situations, such as uncomplicated VSD, PDA, or ASD
7. To evaluate the patient after surgery

C-DOPPLER ECHOCARDIOGRAPHY:

1. A Doppler echo combines the study of cardiac structure and blood flow profiles
2. The Doppler echo allows estimation of pressures in the RV, PA, and LV using the flow velocity of certain valvular or shunt jets.
3. Estimation of PA pressure is particularly important in pediatric patients.

VI -Cardiac Catheterization

The final definitive diagnostic tests for most cardiac patients. They are carried out under general sedation using various sedatives. For newborns, cyanotic infants, and hemodynamically unstable children, general anesthesia with intubation may be used.

Catheters are placed in peripheral (most commonly the femoral) vessels and advanced to the heart and central vessels under fluoroscopy. At each position in the heart and blood vessels, values of pressure and oxygen saturation of blood are obtained. The oxygen saturation data provide information on the site and magnitude of the left-to-right or right-to-left shunt, if any. The pressure data provide information on the site and severity of obstruction. Cardiac output may be obtained from oxygen saturation data

V- ANGIOCARDIOGRAPHY

A radiopaque dye is rapidly injected into a certain site, and angiograms are recorded, often on biplane views. Depending on the cardiovascular anomaly under study, special views are obtained by moving the fluoroscopic camera (or by positioning the patient at desired angles). Multiple injection sites are often necessary to obtain a complete anatomic diagnosis

Indications for these invasive studies

- Selected newborns with cyanotic congenital heart disease (CHD) who may require palliative surgery or balloon atrial septostomy during the procedure
- Selected children with CHD when the lesion is severe enough to require surgical intervention
- Children who appear to have had unsatisfactory results from cardiac surgery
- Infants and children with lesions amenable to balloon angioplasty or valvuloplasty
- Children with hypoplastic or stenotic pulmonary arteries, especially those associated with pulmonary atresia and TOF, with extensive collateral arteries require angiography to delineate the extent of the abnormality.

CHAPTER (IV)

NEPHROLOGY

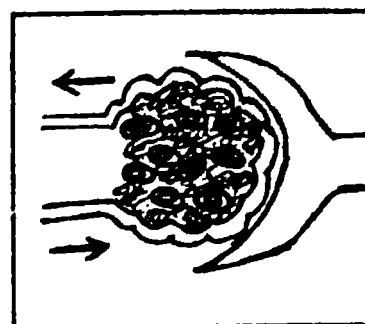
GLOMERULONEPHRITIS (GN)❑ **Definition:**

Inflammation and injury which occur primarily in the glomeruli of the kidney as a result of immunological, inherited or coagulation disorders.

❑ **Microscopic changes**

Different causes of GN produce one of the following changes (some diseases may share the same pathology).

- ❶ Proliferation of the glomerular cells.
- ❷ Crescent formation in Bowman space.
- ❸ Thickening of the glomerular basement membrane.
- ❹ Sclerosis (scarring of the glomeruli).

❑ **Causes of glomerulonephritis:**

- ❶ Acute glomerulonephritis.
- ❷ Chronic glomerulonephritis:
 - ❶ Membranous GN.
 - ❷ Membrano-proliferative GN (MPGN).
 - ❸ Rapidly progressive GN.
- ❸ Glomerulonephritis associated with:
 - ❶ SLE
 - ❷ Henoch Schonlein purpura
 - ❸ Good Pasteure syndrome.

ACUTE GLOMERULONEPHRITIS

"Nephritic syndrome"

Incidence

1. The most common cause of glomerulonephritis. Also called (post-streptococcal GN) as streptococcal infection is the most common cause.
2. Male is more affected than female
3. Age of presentation: 1-7 years.

Aetiology

1. Group A beta-hemolytic streptococci of throat or skin (Nephritogenic strains) are the most common.

	ACGN after throat infec.	AGN after skin infec.
• Strain of strept	→ Type 4, 12	→ Type 49
• Season	→ Winter and spring	→ Summer
• Latent period	→ 1-2 weeks	→ 2-3 weeks
• ASO titre	→ Elevated	→ May be normal

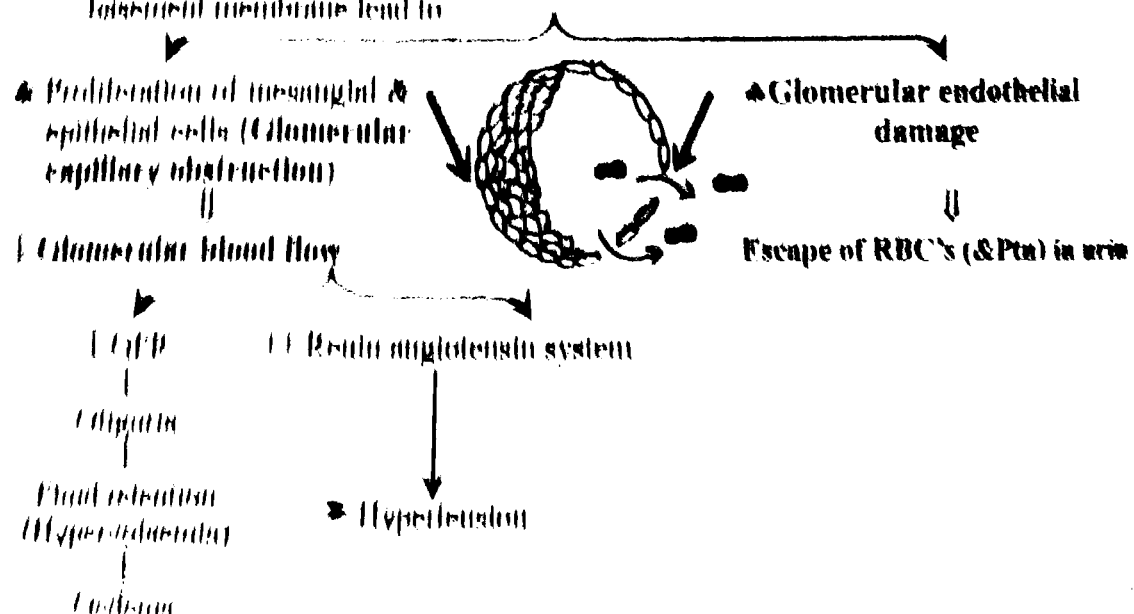
- *N.B.* Few strains of strept. can result in GN so recurrence of post-strept. GN is uncommon and long term prophylaxis is not recommended.

Other infectious agents may be responsible:

- Haem. (pneumococci or staphylococci).
- Virus (Mumps or chicken pox).
- Parasites (Malaria)

Pathogenesis

1. Streptococci (Ag) leads to antibodies (Ab) formation by the body after latent period (1-3 weeks)
2. Ag + Ab + complement → immune complexes which deposited in glomerular basement membrane lead to



❑ Clinical manifestations:

After 1-3 w. of strept. infection sudden onset of the following manifestations develop:

- 1- **Non-specific manifestations:** vomiting, malaise or headache.
- 2- **Mild oedema** (puffiness of eye lids, peripheral oedema) → More in the morning.
- 3- **Smoky dark urine** (Tea or coca cola coloured smoky urine).
- 4- **Oliguria.** (urine output < 1 ml/kg/hour)
- 5- **Hypertension** (50-70%), usually transient (lasts about 1 week).
- 6- **Manifestations of complications** (may be the presenting event).

❑ Complications:

① **Hypertensive heart failure:**

- ⇒ **Due to:** hypertension or hypervolaemia.
- ⇒ **Manifested by:** H.F. or even pulmonary oedema.

② **Hypertensive encephalopathy:**

- ⇒ **Due to:** Cerebral vasoconstriction and cerebral oedema.
- ⇒ **Manifested by:** Headache and vomiting → convulsions → coma.

③ **Acute renal failure:** (Rare)

❑ Investigations:

I- **Urine:**

- ① Colour: Dark red smoky urine which precipitate on standing.
(To be DD from clear red urine of hemoglobinuria).
- ② Volume: ↓↓ (Oliguria)
- ③ Specific gravity: ↑↑.
- ④ Proteinuria (usually not exceed 1 gram / day)
- ⑤ Casts: - RBC's (Diagnostic) as it indicates the renal origin of the bleeding.
- Other casts may be present (cellular, granular and hyaline casts).
- ⑥ Haematuria: Always present and gross.

II- **Blood:**

- 1- Anaemia: Mainly due to hypervolaemia which results in haemodilution, rather than blood loss in urine.
- 2- Electrolyte disturbance: (↑ K, ↑ Ph. and dilutional hyponatraemia).
- 3- Kidney function tests: (May be impaired) → ↑ blood urea (N. 20-40 mg/dl) and creatinine (N 0.2-0.8 mg/dl).
- 4- ↓ Serum complement: (ESP. C₃)
- 5- Evidence of preceding strept. infection:
 - ① +ve throat swab.
 - ② ↑ ASO titre (N. < 1/400) → may be -ve in skin infection.
 - ③ ↑ Anti DNase or anti hyalurodinase if ASO is -ve.

III- **Renal biopsy:**

Not done except if evidences of other aetiology rather than streptococcal are present:

- ① Persistence of hematuria or proteinuria > 2 months.
- ② Normal C₃ or absence of evidence of strept. infection.
- ③ Associated nephrotic syndrome (nephritic nephrosis) or acute renal failure.

□ D.D

1. Other causes of haematuria (see later).
2. Other causes of oedema (see later).
3. Other causes of hypertension.
4. Other causes of encephalopathy.

□ Prevention:

Early systemic antibiotic ttt for streptococcal infection for the proper duration may decrease (but not eliminate) the risk of PSGN.

□ Treatment:

- 1- Bed rest: Til disappearance of manifestations.
- 2- Diet and fluid:
 - Fluid restriction: fluid intake = urine output in the previous day + insensible water loss (400 ml/m²/day)
 - Salt restriction
 - ↓ protein and ↓ K⁺ intake (fruit juice, canned food,)
 - (So the diet is preferably consists of ↑ CHO content)
- 3- Eradication of streptococcal infection:
 - Penicillin (or erythromycin in sensitive cases) for 10 days.
- 4- Treatment of hypertension:
 - Furosemide or thiazides are given.
 - In resistant cases α-methyl dopa, diazoxide or Na nitroprusside can be given.
- 5- Treatment of complications:
 - Treatment of H.F. (Digitalis, Diuretics,)
 - Treatment of ARF if develops (see later)
 - Treatment of convulsions (usually responds to anti-hypertensive therapy) → if not responding anticonvulsants are given.

□ Prognosis:

1. Complete recovery in 95% of cases (Recurrence is rare)
2. Subacute or chronic GIN → renal failure (very rare).
3. Mortality rate < 5%, mainly due to → intractable H.F, brain damage or renal failure.

Q. What leads to massive oedema in nephritis?

- Associated nephrotic (nephritic nephrosis)
- Presence of complications (hypertensive heart failure- acute renal failure).

NEPHROTIC SYNDROME

❑ Definition:

Clinico-laboratory syndrome characterized by:

- ⊙ Heavy proteinuria.
- ⊙ Hypoproteinaemia.
- ⊙ Generalized oedema.
- ⊙ Hyperlipidaemia (Hypercholesterolaemia - ↑triglycerides).

❑ Classification:

I- **Primary nephrotic syndrome (90%)** → Idiopathic nephrotic syndrome.

“Kidney is the involved organ”

- 1- Minimal change nephrotic syndrome (85 %).
- 2- Mesangial proliferation (5%).
- 3- Focal sclerosis (10%).

II- **Secondary nephrotic syndrome:**

“Kidney is affected during the course of systemic illness”

- 1- Glomerulonephritis: commonly with membranous, MPGN
- 2- Collagen diseases: commonly with SLE (lupus nephritis)
- 3- Tumours: Nephrotic syndrome may occur with several extra-renal tumours as carcinomas and lymphomas with unknown mechanism, however production of lymphokines by the tumours may ↑ capillary wall permeability → nephrotic syndrome.
- 4- Drugs: e.g Penicillamine, phenytoin and probencid.

III- **Congenital Nephrotic syndrome** (Nephrosis during the first year of life) is rare and may be due to:

1- **Nephrosis during the 1st 6 months of life:**

- ⊙ Congenital nephrotic S. [Finnish type] → AR/preterm/rapidly progressive.
- ⊙ Congenital infections [TORSCH]
- ⊙ Diffuse mesangial sclerosis of unknown cause.
- ⊙ Drash syndrome [Nephrosis, Wilm's tumour, Genital anomalies].

2- **Nephrosis between 7-12 months of life:**

- ⊙ Idiopathic nephrotic syndrome.
- ⊙ Drugs.

□ Pathophysiology of Nephrotic syndrome:

1- Proteinuria:

- Results from $\uparrow\uparrow$ glomerular capillary wall permeability which may result from loss of negatively charged glycoproteins within the capillary wall.
- Usually massive (> 2 gram/day).
- In minimal change nephrotic syndrome proteinuria is selective (mainly albumin, transferrin & IgG).

2- Hypoproteinaemia:

- Results from loss of protein in urine.
- Total serum proteins < 4.5 gm % (N. 6-8) and Albumin < 2.5 gm% (N.4 gm%).

3- Generalized oedema: Due to:

- a- Hypoalbuminaemia: $\downarrow$ albumin $\rightarrow \downarrow$ plasma oncotic pressure $\rightarrow$ fluid shift from intravascular to extravascular compartment $\rightarrow$ oedema.
- b- Reduction of intravascular volume $\rightarrow$ stimulation of ADH and Aldosterone $\rightarrow$ Na and H₂O retention $\rightarrow \uparrow$ oedema.

4- Hyperlipidaemia: (Almost all lipids e.g. cholesterol and lipoproteins).

- a- Hypoproteinaemia $\rightarrow$ Liver stimulation $\rightarrow \uparrow$ protein synthesis including lipoproteins which do not lost in urine.
- b- $\downarrow$ Lipoprotein lipase $\rightarrow \downarrow$ lipid catabolism $\rightarrow \uparrow$ plasma lipids.

IDIOPATHIC NEPHROTIC SYNDROME

❑ **Definition:** (See before)

The most common cause of Nephrotic syndrome, non inherited, 85% of it present as MCNS.

❑ **Incidence:**

- ⊙ Male: Female (2:1)
- ⊙ Peak age of incidence: 2-8 years.
- ⊙ May follow viral upper respiratory infection so common in winter and spring.

❑ **Aetiology:** Unknown

- 1- **Immune mechanism:** supported by the response of the disease to immuno-suppressive drugs but it is not usually accepted as there is no evidence of immune mediation in pathology or investigations.
- 2- **T-cell abnormality:** → produce circulating factor which ↑ capillary permeability esp. in the kidney (more accepted theory).

❑ **Pathophysiology:** (See before)

❑ **Pathology:** N.B. All types show -ve immunofluorescence.

1- **Minimal change N.S.** (85%)

- ⊙ Light microscopy: Nothing → so called Nil-type
 - ⊙ Electron microscopy: Fusion of the foot processes of the epithelial cells lining the basement membrane
- (This type has the best prognosis and > 95% of cases respond to steroid therapy).

2- **Mesangial proliferation** (5%)

- ⊙ Light microscopy: mesangial proliferation but no scarring
 - ⊙ Electron microscopy: confirm the data.
- (This type has intermediate prognosis with response to steroids in 50-60% of cases).

3- **Focal sclerosis** (10%)

- ⊙ Light microscopy: mesangial proliferation in glomeruli with scarring (sclerosis) of some of them.
 - ⊙ Electron microscopy: confirm the data.
- (This type has the worst prognosis, usually not respond to steroids and CRF is the rule).

❑ **Clinical manifestations:**

1- **Generalized oedema:**

- ⊙ Begins in the face (periorbital puffiness) then progress to involve the lower limbs, abd. wall and scrotum. Ascitis and pleural effusion are common.
- ⊙ Oedema of intestinal mucosa may lead to vomiting, anorexia and diarrhea.

2- **Manifestations of complications.**

3- **Haematuria and hypertension:** are not present. If present they may suggest nephritic nephrosis or a pathology rather than MCNS.

□ Complications:

1- ↑ Tendency for vascular thrombosis:

Due to: ☹ ↓ antithrombin III level.

- ☹ ↑ certain coagulation factors & platelet aggregation.
- ☹ Haemoconcentration (Fluid is extravascular).

Common Sites: Renal vein thrombosis/DVT/cerebral thrombosis.

2- ↑↑ Tendency for infection:

Due to: ☹ Oedema fluid acts as a culture for the organisms

- ☹ Loss of immunoglobulins and properdin factor B in urine.
- ☹ ↓ splenic function due to hypoperfusion of the spleen.
- ☹ Immuno suppressive therapy.

Common organisms: Pneumococcal then gram -ve bacteria.

Common Sites: Peritonitis then pneumonia, UTI and sepsis.

3- Renal function deterioration:

Very rare in MCNS but occurs in other types.

4- Relapse:

- ☹ Very common in all types and not affect the prognosis.
- ☹ Defined as recurrence of proteinuria for 3 successive days or reappearance of oedema.

5- Complications of TTT:

A- Steroids:

- General: cushinoid face, buffalo hump, obesity.
- CNS: psychic problems.
- CVS: hypertension.
- GIT: peptic ulceration.
- Skin: poor healing of wounds, stria, ↑ hair.
- Skeletal: osteoporosis, growth retardation.
- Metabolic: hyperglycaemia and suppression of suprarenal gland
- Immunological: ↓ resistance to infection and activation of T B
- Eye: cataract.

(The use of tapering and alternate day therapy decrease these side effects)

B- Diuretics:

- Hyponatraemia
- Hypotension
- Hypokalaemia
- Severe hypovolaemia (may lead to hypovolaemic shock)

C- Cyclophosphamide:

- Alopecia.
- Bone marrow depression
- Haemorrhagic Cystitis
- Sterility.

□ Investigations:

I- Urine:

- Colour: Normal
- Volume: ↓↓ (Oliguria)
- Specific gravity: ↑↑.
- Proteinuria: Heavy i.e. nephrotic range proteinuria (> 2 gram / day, > 40 mg/m²/hr or urine protein/ creatinine ratio > 2 .) and selective in MCNS.
- Casts: Lipoid casts ± granular casts.
- Haematuria: Rare, if present it is usually microscopic

II- Blood:

- 1- ↓ Serum proteins (< 4.5 gm/dl) and albumin (< 2.5 gm/dl).
- 2- ↑ Serum cholesterol (> 250 mg/dl).
- 3- Normal serum complement (normal C₃).
- 4- Kidney function tests (usually normal).
- 5- ↑ ESR.

III- Renal biopsy:

Not done except if other cause rather than MCNS is suspected.

- Age: < 1 year or > 8 years.
- Associated ↓ C₃ or gross hematuria.
- Failure to respond to steroids.

□ D.D:

I- A case of oedema so must be D.D. from other causes of generalized oedema:

	Renal	Cardiac	Hepatic	Nutritional	Angioneurotic
♦ Age	Childhood	Any	Any	Infancy	Any
♦ Site of appearance	Eye lids	Lower limb (sacrum in bed ridden)	LL (± ascitis)	Dorsa of hand and foot	Lips and cheeks.
♦ Ascitis	+	+	+	-	-
♦ Associated manifestations	- Urinary manifestations ± Oliguria or hematuria	- Tachypnea - Tachycardia - Tender liver - History of cardiac lesion	- Jaundice - Rt. abd. pain - Splenomegaly - History of liver disease.	- Growth retardation - Muscle wasting - mental affection	- Itching - History of exposure to allergen
♦ Investigations	- Urine - KFT	- ECG - ECHO	- Sonar - LFT	- History	- History

II- This renal oedema must be D.D. from other causes of renal oedema:

- ⊙ Nephritic syndrome
 - ⊙ Renal failure
- } ⇒ Discuss

III- The case of renal oedema proved to be Nephrotic so MCNS must be DD from other causes of nephrotic syndrome:

	MCNS	Other types of Nephrotic S.
• Hematuria	- Minimal or absent	- May present
• Proteinuria	- Selective (Albumin and IgG)	- Less selective
• Serum C ₃	- Normal	- May be ↓↓
• Steroid response	- Good	- Variable
• Renal biopsy	- not needed but diagnostic	- Confirm

□ Management of nephrotic syndrome:

1- Hospitalization and monitoring for:

- ⊙ Urine output
- ⊙ Progress of oedema.
- ⊙ Blood pressure
- ⊙ Signs of infection.

N.B. Some authors recommend postponing steroid treatment for one week to treat latent infection and also spontaneous resolution may occur.

2- Diet:

- ⊙ Salt restriction and fat better avoided (nauseating).
- ⊙ Excess Ptn., CHO and Potassium supplementation.
- ⊙ Fluid restriction if there is progressive weight gain. Fluid intake = urine output in the previous day + insensible water loss (400 ml/m²/day)

3- Antibiotics:

- ⊙ Broad spectrum antibiotics are given if there is high incidence of suspension of having infection until results of culture and sensitivity (symptoms usually mild as the patient is immune compromised).
- ⊙ Avoid nephrotoxic drugs.

4- TTT of oedema: (If massive)

Salt free albumin:

In massive oedema → 1 gm/kg I.V. infusion over 8 hours followed by lasix (Frusemide) to avoid hypervolaemia.

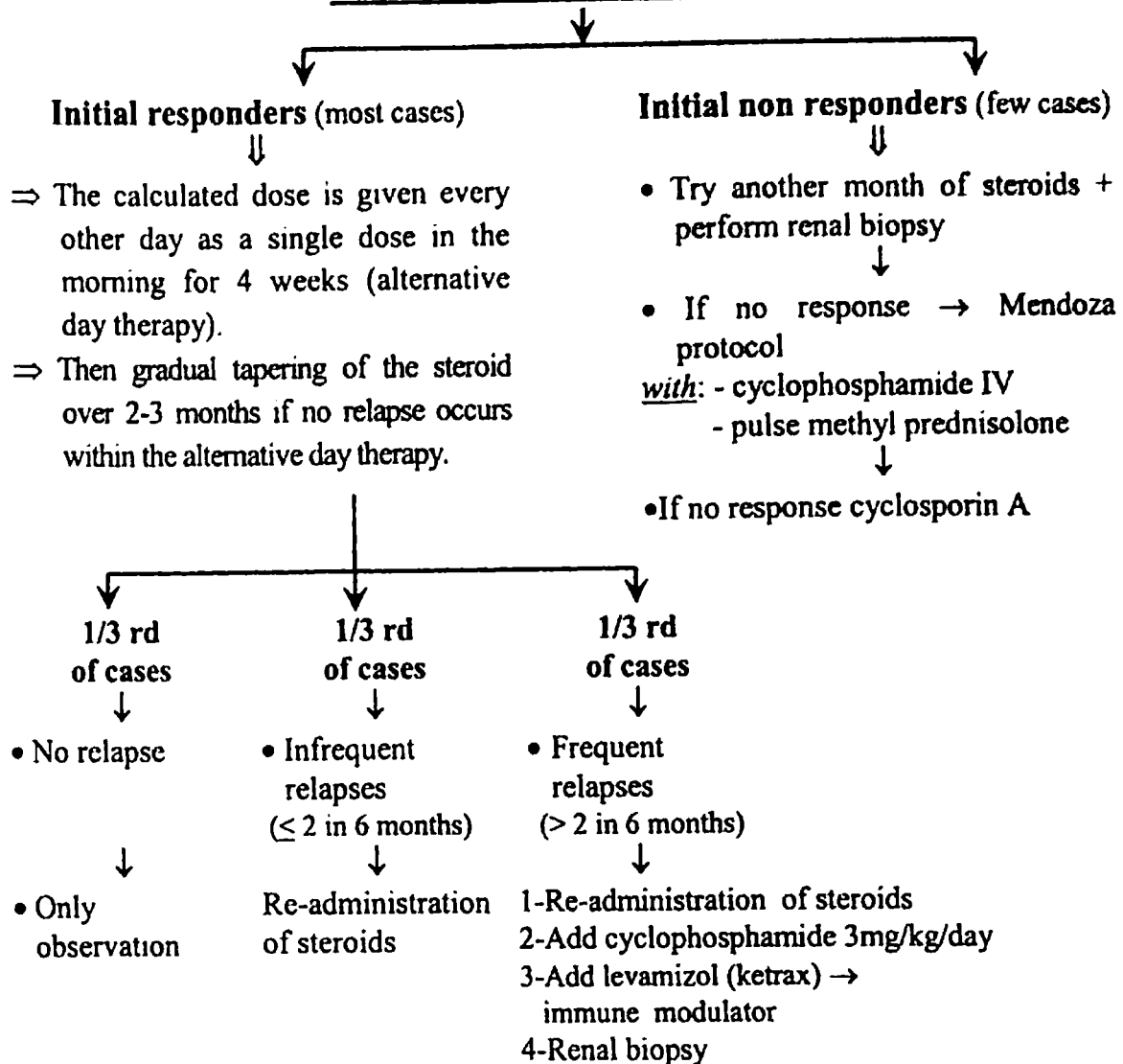
5- Prevention of complications:

- Low dose aspirin → ↓ risk of thrombosis
- Pneumococcal, varicella & Hib vaccine → after remission.

6- Specific ttt:

- Prednisone (Hostacortin 5 mg tab) is used in a dose of 2 mg/kg/day → maximum 60 mg/day (12 tab).
- The total dose is divided in 3 doses per day for one month in order to achieve remission (5 days urine free from proteins).

Response to one month steroids



N.B. Drug therapy has a lot of side effects (mention)

□ **Prognosis:**

- 1- Most cases respond to steroid with complete resolution after infrequent or frequent relapses (remission and relapse may continue for years before complete remission which is usually achieved by the 2nd decade of life).
- 2- About 10% progress to CRF (usually of the non MCNS types)

RENAL FAILURE**ACUTE RENAL FAILURE (ARF)****□ Definition:**

Clinico-laboratory syndrome results from acute impairment of renal function, chch by:

- 1- Anuria or oliguria (urine $< 180 \text{ ml/m}^2/\text{day}$)
- 2- Electrolyte and acid base disturbance.
- 3- $\uparrow$ Blood urea and creatinine.

□ Pathogenesis:

ARF may be divided into 3 categories:

	Pre renal causes	Renal causes	Post renal causes
Aetiology $\rightarrow$	Causes of $\downarrow$ renal perfusion: 1- Dehydration 2- Hge and shock 3- Hypotension 4- Burn.	1-Acute tubular necrosis e.g drugs & untreated pre-renal causes. 2-Acute glomerulonephritis 3-Acute interstitial nephritis 4-Hemolytic- uraemic syndrome 5-Renal vein thrombosis	1- <u>Congenital</u> : - Post. urethral valve - Congenital stricture of urethra or both ureters. 2- <u>Acquired</u> : - Stones - Tumours
Mechanism $\rightarrow$	- Hypovolaemia $\rightarrow \downarrow$ renal perfusion $\rightarrow$ ++ renin/angiotensin $\rightarrow$ Vasoconstriction $\rightarrow$ More $\downarrow$ of renal blood flow $\rightarrow \downarrow$ GFR (Transient but if prolonged renal damage is permanent)	- Direct damage of the renal tissues by the disease	- Obstruction to urine outflow leads to back pressure on both kidneys $\rightarrow \downarrow$ GFR and gradually $\uparrow$ renal tissue damage.

□ Pathophysiology:

- 1- **Hyper-kalaemia:** This develops because of: decreased renal excretion of K^+ , cellular release of K^+ as a result of metabolic acidosis, infection, trauma, hemolysis or hypoxia.
- 2- **Water overload & hyponatremia:** Water overload is due to reduced Na excretion, this lead to interstitial edema, pleural effusion, hypertension, circulatory congestion and pulmonary edema. Hyponatremia if present is the result of dilution of body fluids as a consequence of excessive intake of water relative to that of Na.
- 3- **Metabolic acidosis:** This reflects impaired ability of the kidney to eliminate acid ions as well as increased catabolic production of acids.
- 4- **Hypocalcaemia:** may occur as a result of hyperphosphatemia.
- 5- **Hypertension:** may develop consequent to Na, H_2O retention. It may result in hypertensive encephalopathy or aggravate circulatory congestion.
- 6- **Blood:** Urea, uric acid, phosphate and serum creatinine are increased because of decreased excretion.

□ Clinical manifestations:

1- Manifestations of the cause:

2- Oliguric phase:

- ☉ *Early ARF:*
 - Oliguria or anuria
 - Hypertension
 - Oedema
 - Acidotic breathing
- ☉ *Advanced ARF:*
 - Cardiac (H.F. ± pulmonary oedema)
 - CNS (convulsions ± uraemic encephalopathy)
 - GIT (Bleeding) → due to stress ulcer + thrombocytopenia
 - Electrolytes (arrhythmia due to ↑K),
(tetany is rare despite ↓Ca due to acidosis).

3- Diuretic phase: It indicates early recovery in which the tubules becomes patent but unable to retain fluids so polyuria with loss of electrolytes occur till complete return of renal function.

□ Investigations:

- 1- Kidney Function Tests: ↑ blood urea (N. 20-40 mg/dl) & creatinine (N. 0.2-0.8 mg/dl)
- 2- Acid base disturbance: Metabolic acidosis (↓PH, ↓ HCO₃, ↓ PaCO₂).
- 3- Electrolyte imbalance:
 - ☉ Hyperkalaemia, hyperphosphatemia
 - ☉ Hypocalcaemia, hypo Na (dilutional).
- 4- Investigations for the cause:
 - ☉ Laboratory: ASO titre, CBC, C₃,
 - ☉ Radiological: X-ray, IVP, Abd. sonar.
 - ☉ Renal biopsy: If indicated.

□ Management of ARF:

I- Treatment of post-renal causes of ARF:

Surgical consultation

II- Treatment of pre-renal failure:

- 1- *Volume expanders* are given [saline, ringer lactate or plasma] 20-30 ml/kg in 1/2-1 hour then assessment of hydration, if not adequate, volume expanders may be repeated.
- 2- *After full hydration:* the patient must pass urine within 2 hours.
- 3- If the patient is fully hydrated and passed no urine after 2hrs → *Diuretics*
(Frusemide 2 mg/kg/I.V. may be repeated or mannitol 20% 1/2 gm/kg/I.V. infusion).
- 4- *If no improvement* the condition is treated as renal causes of ARF.

III- Treatment of renal causes of ARF:

- 1- *Hospitalization* with monitoring of urine output, BP, pulse and oedema.
- 2- *Diet and fluids:*
 - ☉ Fluid restriction in oliguric state:
(fluid intake = urine output in the previous day + insensible water loss)
 - ☉ Oral diet must be nutritious and light. Na⁺ and K⁺ should be avoided.
 - ☉ I.V. fluids may be indicated if unconscious patient (but must be restricted).
 - ☉ In diuretic phase excess fluids and electrolytes intake is advisable.
- 3- *TTT of metabolic acidosis:*
 - ☉ In mild cases No correction is required
 - ☉ In severe cases (PH < 7.2) → Na HCO₃ 5% (1-2 ml/kg I.V.).

4- TTT of electrolyte disturbance

• Hyperkalaemia:

- Kayxalate (Na exchange resin) → oral or enema.
- Glucose: Insulin infusion → (leads to intracellular shift of K^+).
- $NaHCO_3$ → correct acidosis (leads to intracellular shift of K^+).
- Salbutamol → IV or neubelizer (leads to intracellular shift of K^+).
- Ca gluconate 10% → counteract the cardiac effects of hyperkalaemia.
- Dialysis → in resistant cases.

• Hyponatraemia:

Usually dilutional so responds to fluid restriction.

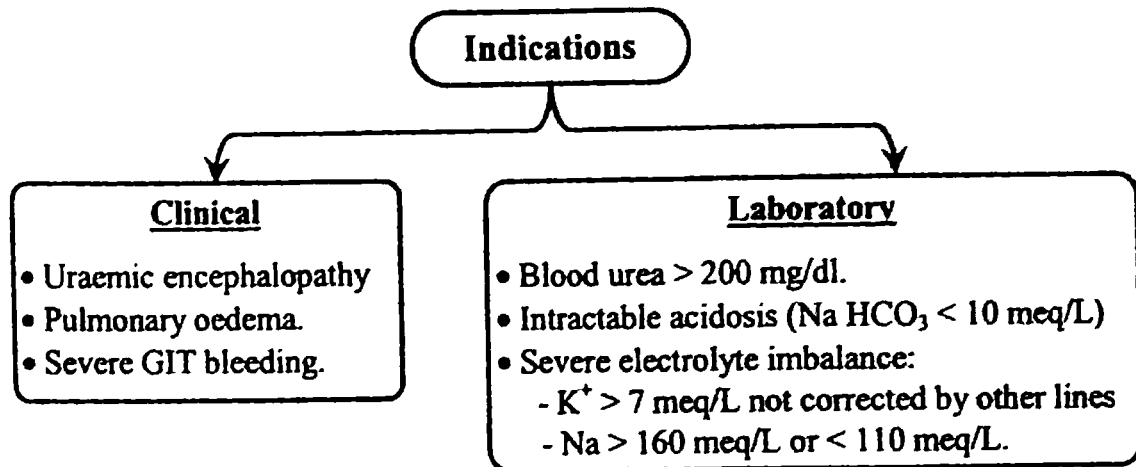
• Hypocalcaemia and hyperphosphataemia:

Treated by with oral Ph. binders (Ca carbonate better than aluminum hydroxide).

5- TTT of complications:

- Anaemia (packed RBC's)
- Stress ulcer (antacids + H_2 receptor blockers)
- Infection (Non nephrotoxic antibiotics).
- Hypertension (see GN).

6- Dialysis either peritoneal or haemo dialysis



□ Prognosis:

- Better in pre-renal.
- In renal depends on the cause.

CHRONIC RENAL FAILURE

□ Definition:

Complex clinical - biochemical and metabolic disturbances resulting from permanent reduction of GFR below $20 \text{ ml/m}^2/\text{min}$. (normally GFR = $70 \text{ ml/m}^2/\text{min}$. in 1-3 yrs child).

□ Causes:

- 1- Congenital renal anomalies: e.g. bilateral renal dysplasia, bilateral vesico-ureteric reflux, congenital obstructive uropathy, congenital nephrosis,
- 2- Chronic glomerular disease:
 - MPGN
 - SLE
 - Rapidly progressive GN
- 3- Chronic renal infection:
 - Chronic pyelonephritis
 - Chronic interstitial nephritis

□ Manifestations:

- ✱ Insidious progressive manifestations (so difficult in diagnosis).
- ✱ Multisystem involvement:
 - Renal osteodystrophy (rickets) $\Rightarrow$ see glomerular rickets.
 - Growth failure.
 - Hypertension.
 - Chronic anaemia (anemia of chronic renal failure due to $\downarrow$ erythropoietin).
 - Polyuria & polydipsia.
 - Uraemic manifestations:
 - Anorexia & malaise.
 - Pericarditis & cardiomyopathy
 - Chronic vomiting & hicough.
 - Drowsiness $\rightarrow$ coma

□ Investigations:

- $\downarrow$ GFR.
- The same investigations as ARF.

□ Treatment:

- Conservative management (good diet - recombinant erythropoietin - vit. D & Ca).
- Regular hemodialysis
- Renal transplantation in child > 5 yrs with end stage RF.

HEMOLYTIC UREMIC SYNDROME

- ❑ **Def.** Systemic disease chch by hematological defect with 2ry renal involvement.
- ❑ **Incidence:**
 - ⊕ Children aged (4 months – 4 years).
 - ⊕ The commonest cause of ARF below 4 years.
- ❑ **Aetiology:**
 - 1- **Diarrhea +ve HUS:** (most cases) following GE due to verotoxin producing strain of E-coli O157:H7, sometimes campylobacter & shigella (all associated with bloody diarrhea).
 - 2- **Diarrhea -ve HUS:** few cases may be 2ry to SLE, drugs, URTI or familial.
- ❑ **Pathogenesis:**
 - 1- Any of the above causes may lead to ↑ some factors (TNF – Interleukins) which ↑↑ platelet aggregation & procoagulants → localized thrombi in glomerular capillaries → obstruction of renal vasculature.
 - 2- Obstruction of renal vasculature:
 - Renal insufficiency → Haematuria & ARF
 - Damage of circulating RBC's and platelets (Microangiopathic hemolytic anaemia and thrombocytopenia).
- ❑ **Clinical manifestations:**
 - 1- Acute onset after 10 days from GE or URTI.
 - 2- Manifestations of acute hemolysis (Pallor, jaundice ± dark urine).
 - 3- Hematuria and manifestations of ARF (Oliguria, oedema, hypertension & acidotic breathing) usually develop.
- ❑ **Investigations:**
 - 1- Thrombocytopenia, but normal PT, PTT (D.D. DIC).
 - 2- Blood film → fragmented RBC'S (Helmet's cells).
 - 3- Investigations for acute hemolysis (↓ Hb, ↑RC) with –ve Coomb's test.
 - 4- Investigations for ARF (↑ urea, creatinine).
 - 5- Urine analysis (hematuria & hemoglobinuria)
- ❑ **D.D.:**
 - 1- **Causes of microangiopathic Hemolytic Anaemia and thrombocytopenia**
 - DIC • Renal vein thrombosis • SLE • Malignant hypertension.
 - 2- **Causes of ARF** (see before).
- ❑ **Prevention:**

Proper cooking of meat (hamburger).
- ❑ **Treatment:**
 - 1- **TTT of ARF** (see before) → esp. dialysis.
 - 2- **Blood transfusion** in severe ↓ of Hb (<6 gm %) and **plasma transfusion**.
 - 3- **Heparin** (anticoagulant) → controversial.

URINARY TRACT INFECTION (UTI)**□ Definition:**

A disease of clinical symptomatology and bactiruria results from infection of upper urinary tract (pyelonephritis) or lower urinary tract (cystitis or urethritis).

□ Incidence:

① **Age:** ☆ Common at any age esp. the first year of life.

☆ Very young infants are more susceptible to UTI due to:

- Umbilicus may be a portal of infection.
- Poor resistance of the newborn.
- Faecal contamination is too much common.

② **Sex:** ☆ Neonatal & early infancy (Male = female).

☆ After that more common in female (female : male = 9:1) due to short urethra & easily ascending of the perineal organisms to the urinary tract.

□ Aetiology:

☆ **Organism:**

- 1- E.coli (80 - 90%).
- 2- Other gram -ve bacteria (Klebsiella, proteus,).
- 3- Gram +ve bacteria (staph aureus, strept faecalis,).
- 4- Rarely adenovirus & candida albicans.

☆ **Route of infection:**

- 1- Ascending infection via the urethra (the commonest).
- 2- Haematogenous or lymphatic spread (uncommon).

☆ **Predisposing factors:**

1- **Factors resulting in urinary stagnation:**

- Vesico - ureteric reflux ⇒ the most common PPF.
- Infrequent micturation & inadequate fluid intake → ↓ urinary output.
- Obstruction ⇒ posterior urethral valve, ureteric stricture, stones.

2- **Factors facilitate ascent of the organism through urethra:**

- Urinary catheterization.
- Urethral and bladder surgery.
- Frequent stool contamination in the perineum.

3- **Factors ↓↓ the immunity of the child:**

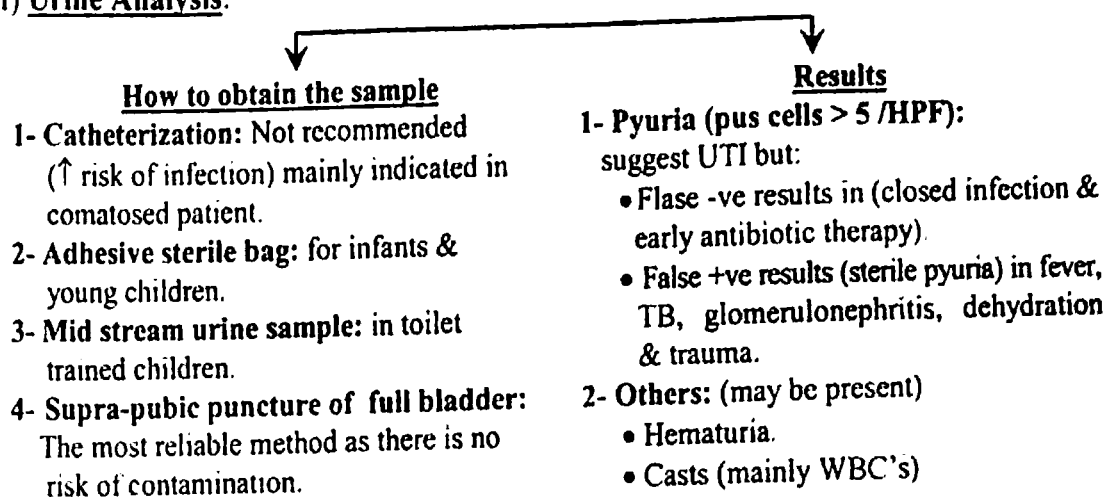
- Diabetes mellitus.
- Debilitating illness.
- Immuno suppressive drugs.

□ Clinical Manifestations:

- 1- Asymptomatic: Accidentally discovered in urinalysis (Esp. recurrent UTI).
- 2- Newborn: Jaundice, irritability $\pm$ fever (Non specific manifestations).
- 3- Infants:
 - Fever, vomiting, wt. loss, failure to thrive.
 - Screaming during micturition.
- 4- Children:
 - Urinary symptoms (dysuria, urgency, frequency).
 - 2ry nocturnal enuresis.
 - May be haematuria or hypertension.
 - General: fever, rigors $\pm$ flank pain (esp. in upper UTI).

□ Investigations:

I) Urine Analysis:



II) Urine Culture: to detect bacteruria

- ☆ According to colony count:
 - 1- Colony count $> 10^5$ /ml $\Rightarrow$ UTI
 - 2- Colony count $10^4 - 10^5$ /ml $\Rightarrow$ repeat the sample.
 - 3- Colony count $\leq 10^3$ /ml $\Rightarrow$ contamination (No UTI)
- ☆ If +ve colony count ($> 10^5$ /ml) is present, sensitivity to antibiotics is tested to choose the proper antibiotic.

III) Supportive evidences:

- 1- Blood picture $\rightarrow$ leukocytosis.
- 2- CRP $\rightarrow$ may be +ve.
- 3- Blood culture (sepsis) $\rightarrow$ may be +ve.

IV) Investigations for recurrent UTI:

- 1- *Abd. x-ray & sonar & IVP* : to detect obstruction in urinary tract.
- 2- *Micturating cystourethrogram* : for vesico-ureteric reflux.
- 3- *Renal scanning & kidney function* : to evaluate renal function.

□ Treatment of UTI:

1- General lines:

- Excess fluid intake.
- Antipyretics for fever.
- Regular & complete emptying of the bladder.

2- Antibiotics:

- Must be given according to urinary culture and sensitivity tests for at least 2 weeks.
- While waiting for the culture:

(I) *Mild to moderate infection*

oral

- Co-trimoxazole (24 mg/Kg/day $\Rightarrow$ 2 doses)
- or • Nitrofurantoin (5 mg/Kg/day $\Rightarrow$ 3-4 doses)
- or • Amoxicillin (50 mg/Kg/day $\Rightarrow$ 3-4 doses)

(II) *Severe infection in acutely ill child:*

IV Combination of

- Ampicillin (100 mg/Kg/day $\Rightarrow$ 3-4 doses).
- Gentamycin (5 mg/Kg/day $\Rightarrow$ 2-3 doses).

or 3rd generation cephalosporins (100 mg/Kg/day $\Rightarrow$ 2 doses)

N.B. $\rightarrow$ gentamycin is nephrotoxic so renal function must be monitored during treatment.

3- Follow up:

- ☆ Urine culture after one week of termination of treatment to ensure recovery.
- ☆ Urine culture every 3 months for one year to diagnose recurrent UTI which is usually asymptomatic.

4- Management of recurrent UTI:

- ☆ Treatment of the underlying problem (stone, vesico-ureteric reflux, stricture,.....).
- ☆ Full course of antibiotic therapy.
- ☆ Then $\Rightarrow$ long term prophylaxis using co-trimoxazole in low dose (1/3 rd of the usual) single daily dose for 6 months.

□ Prognosis:

- ⊗ The long term prognosis is usually good especially in early diagnosis and treatment.
- ⊗ In untreated and neglected cases renal failure may occur later in life.

URINARY SYMPTOMATOLOGY

CAUSES OF HAEMATURIA

(> 5 RBC's / HPF in urine)

1- Pre-renal:

- (I) Hemorrhagic blood diseases:
(Platelet, Vascular & Coagulation) defects
- (II) Hemorrhagic fevers.

2- Renal:

- (i) All causes of glomerulonephritis (mention)
- (ii) Developmental renal anomalies (e.g. polycystic kidney).
- (iii) Renal tumours & cysts
- (iv) Renal vein thrombosis
- (v) Haemolytic - uremic syndrome.

3- Post Renal:

- (i) Trauma.
- (ii) Urinary stones.
- (iii) UTI.

4- Others

- (i) Bilharziasis.
- (ii) Exercise induced hematuria.
- (iii) Drugs e.g. cyclophosphamide.
- (iv) Infective endocarditis (embolic).

CAUSES OF PROTEINURIA

(Ptn > 150 mg/day in urine)

Non pathological

1- Decubital (orthostatic)

proteinuria in standing which disappear in supine position.

2- Exercise proteinuria

↑ urinary protein may follow vigorous muscular exercise in some children

3- Febrile proteinuria

↑ urinary proteins may be found after temp. > 38.5 in some children

Pathological

TUBULAR

1- Inherited

- Fanconi
- Fanconi like syndromes
- Renal tubular acidosis.

2- Acquired:

- Drugs (analgesics, antibiotics,.....).
- Interstitial nephritis.
- Hypokalaemia.
- Acute tubular necrosis.

GLOMERULAR

1- Nephrotic syndrome

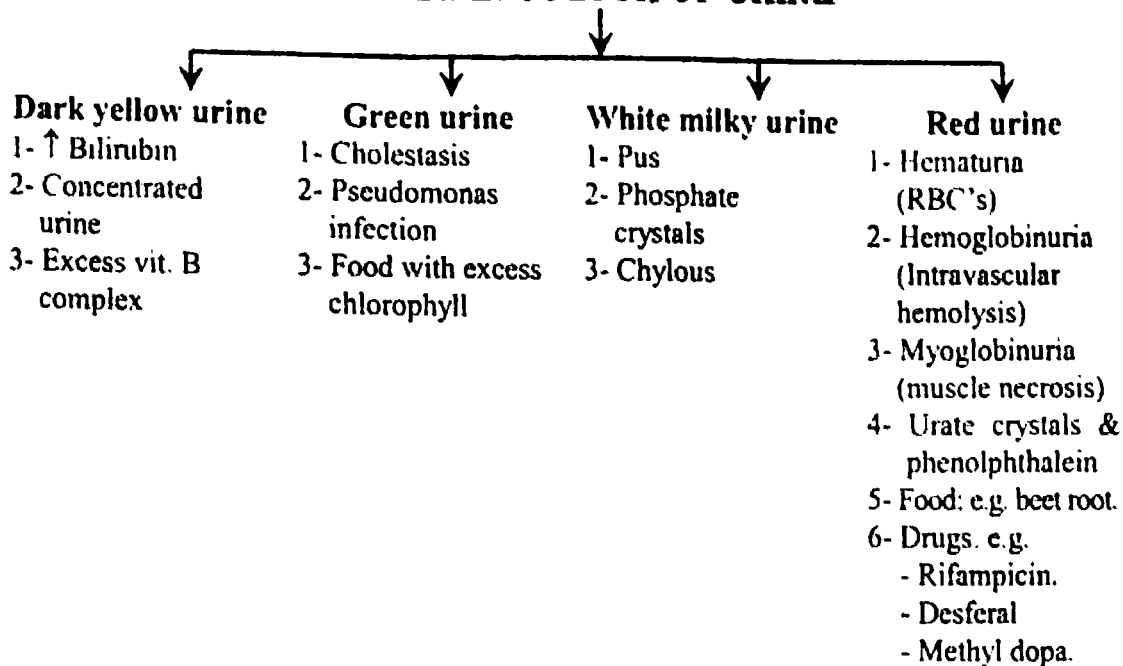
2- Glomerulonephritis

3- Persistent asymptomatic

N.B.: Proteinuria is classified into:

- Mild (150 - 500 mg/d) ⇒ e.g. tubular proteinuria.
- Moderate (500 - 2000 mg/d) ⇒ e.g. PSGN
- Severe (> 2000 mg/d) ⇒ Mainly in Nephrotic syndrome.

CHANGE IN COLOUR OF URINE

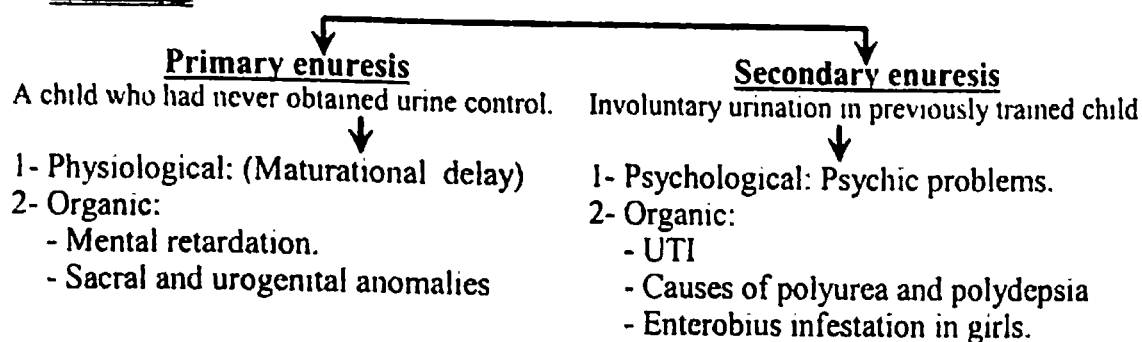


ENURESIS

❑ **Definition:** Involuntary urination after 4 years age.

❑ **Types:** 1- Nocturnal (Night wetting) 2- Diurnal (Daytime wetting)

❑ **Aetiology:**



❑ **Investigations:**

Urine analysis and culture, stool analysis (enterobius), blood glucose and x-ray spine .

❑ **Treatment:**

1- **TTT of the cause:** e.g. ttt of UTI, psychotherapy if needed, ...

2- **Simple measures:**

- * The child is prohibited from drinking after dinner and avoid punishment.
- * The child must urinate before sleep and awaken by night to urinate.
- * Bladder exercises (e.g. stream interruption and urine holding).

3- **Drug therapy:** In failure of the above lines:

- * Tricyclic antidepressants → Tofranil tab. (oral).
- * Desmopressin → Minirin (intra nasal inhalation, injection or oral).

4- **Enuresis Alarm:** In resistant cases.

SYSTEMIC LUPUS ERYTHEMATOSIS

□ Def.:

Multisystem inflammatory disease caused by deposition of soluble immune complexes in various tissues.

□ Incidence:

- Female : male (8 : 1).
- Common between (9-15) years

□ C/P:

- ① Systemic manifestations (Anorexia, fever, wt. loss,)
- ② Neurological (psychosis, fits & neuropathy).
- ③ Skin lesions (Butterfly erythema, alopecia, Raynaud's phenomenon,)
- ④ Endocarditis.
- ⑤ Polyserositis (pleurisy, peritonitis & pericarditis).
- ⑥ HSM & LN ++
- ⑦ Renal SLE ⇒ progressive & the leading cause of death.
- ⑧ Arthritis.



□ Invest:

- ☛ Hematological → leukopenia, thrombocytopenia & hemolytic anaemia.
- ☛ +ve antinuclear antibody (ANA) & more specific anti-double stranded DNA antibody
- ☛ ↓ complement (↓ C₃)
- ☛ For the effect of SLE (e.g ECHO / Renal biopsy).

□ TTT:

- Steroids(starting with pulse methyl prednisolone).
- Immuno suppressive drugs (cyclophosphamide or azathioprine)

CHAPTER (V)

GIT AND HEPATOLOGY

VOMITING IN INFANCY AND CHILDHOOD

<u>Acute vomiting</u>	<u>Chronic or recurrent vomiting</u>
1- Acute infections: CNS/ Respiratory / Abdominal (GE) / Renal / Pancreatitis / Septicaemia 2- Acute metabolic conditions: * Diabetic keto-acidosis * Acute toxicity (drugs & foods) * Ryc syndrome 3- Acute intestinal obstruction: (Bilous vomiting + Abdominal distention + Absolute constipation) * Functional (ileus) * Organic (Intussusception / volvulus / strangulated hernia)	1-Feeding disorders: * Over feeding * Milk allergy. 2- Chronic metabolic conditions: * Chronic renal failure * Hypercalcaemia * Metabolic disorders 3- GIT Causes: * Cardiac Achalasia * GERD * Hiatus hernia * Pyloric stenosis * Peptic ulceration 4- ↑↑↑ ICT: e.g. meningitis, encephalitis,

ABDOMINAL PAIN IN INFANCY AND CHILDHOOD

<u>Acute abdominal pain</u>	<u>Chronic or Recurrent abd. pain</u>
1- Acute abd. Infection: * Streptococcal pharyngitis: due to mesentric adenitis * Early G.E. * Acute pancreatitis. * Acute pyelonephritis. * Acute appendicitis. * Acute peritonitis. * Acute hepatitis (due to stretch of liver capsule). 2- Acute intestinal obstruction: "See vomiting" 3- Acute medical conditions: * Henoch Schonlein purpura * Diabetic keto-acidosis * Rheumatic fever (Rh. peritonitis) * Acute intoxication * Pneumonia (Lower lobe)	1- Functional "Irritable bowel syndrome" More than 90% of causes. May be related to family stress or psychic problems 2- Organic causes "Rare" Common * Parasites (Giardia, amoeba) * Chronic constipation * Chronic diarrhea Uncommon * Chronic hepatitis * Peptic ulceration H.pylori related problems. * Renal stones

Intussusception

! Definition:

Invagination of one portion of the intestine into a more distal portion resulting in impairment of the blood supply leading to necrosis of the involved segment of the bowel (gangrene).

! Clinical picture:

Age: 5 month -1 year, the infant is usually healthy and well nourished.

- 1-Sudden onset of recurrent sharp abdominal pain (Screaming attacks).
- 2-Bleeding per rectum and vomiting becomes progressive.
- 3-Pallor, mild dehydration and mild fever.
- 4-Sausage shaped mass in the right upper quadrant of the abdomen.
- 5-Red current jelly stools can be seen especially on rectal examination.

! Investigations:

- 1-X-ray with signs of intestinal obstruction → multiple fluid levels.
- 2-Abdominal ultrasound.

! Treatment:

- 1-Surgical by simple reduction, but if gangrenous loop is present resection anastomosis.
- 2- Fluid and electrolyte therapy before operation.

N.B : Hydrostatic reduction by barium enema may be attempted in simple cases.

Stomatitis

! Definition:

Inflammation of the oral mucous membrane.

! Types :

A) Catarrhal stomatitis:

mild generalized inflammation of the oral mucous membrane. It accompanies acute infections as measles or may be due to local factors (chemical, traumatic or thermal).

-Treatment: no specific treatment (gentian violet 1% may be used)

B) Herpetic gingivo-stomatitis:

- Caused by herpes simplex virus.
- Clinical picture: acute onset of fever, anorexia followed after few days by the appearance of herpetic vesicles which are flattened and may rupture leading to the formation of ulcers. The condition is associated with pain, excessive salivation, bad odor of the mouth and the gums may be swollen and bleed.
- Treatment:
 - 1- Care of feeding: The infant is given cold fluids; a nasogastric tube may be needed in severe cases.
 - 2- Mouth paint with gentian violet 2% or silver nitrate 2%.
 - 3- Antiviral agents as Acyclovir (Zovirax) may be used (but expensive).

C) Thrush stomatitis (Monillias):

- Due to infection of the buccal mucosa by candida albicans.
- The condition occurs in new born: infected from the mother (genital moniliasis) or by infected teats, malnourished infants due to decreased cell mediated immunity or as a side effect of excess use of antibiotics.
- Clinical picture: numerous small white flakes on the dorsum of tongue, inner side of cheeks and on the palate. In extensive cases a thick white membrane not easily removed is seen on dorsum of tongue (must be differentiated from milk curd).
- Prevention: The nipple and areola of the mother should be cleaned before feeding and painted with nystatin ointment in between meals.
- Treatment:
 - Nystatin drops 3-4 times/day (for 7-10 days).
 - Miconazol gel 3-4 times/day (for 7-10 days).

D) Gangrenous stomatitis (cancrum oris):

- A condition that occurs in severely debilitated children with diseases as measles. A deep large ulcer on the inner surface of the cheeks that spread slowly by necrosis of adjacent tissues. It may lead to perforation of the cheek.
- Treatment: antibiotics plus surgical excision of necrotic areas.

CARDIAC ACHALASIA

! Definition:

Failure of relaxation of LES with swallowing. Most cases occur after 15 yrs old.

! Aetiology:

Absence of the ganglionic cells in the LES $\Rightarrow$ persistent block of LES.

! C/P:

1. Dysphagia to liquids (Solids open LES by weight & gravity).
2. Regurgitation, vomiting and chronic cough (aspiration).
3. In progressive cases $\Rightarrow$ Failure to thrive & emaciation.

! Investigation:

1. X-ray barium swallow $\Rightarrow$ Markedly dilated esophagus with tapered lower end.
2. Esophageal manometry $\Rightarrow$ Measures LES pressure ($\uparrow\uparrow$).

! Treatment:

1. Medical ttt by Ca channel blockers or local injection of botulinum toxin.
2. Dilatation of the LES (by bags or air).
3. In resistant cases surgery is indicated (Heller Myotomy).

GASTRO- ESOPHAGEAL REFLUX DISEASE

GERD “Chalasia”

! **Definition:**

Abnormal retrograde passage of gastric contents into the esophagus commonly occurs in neonates and young infants.

! **Aetiology:**

Persistent relaxation of lower esophageal sphincter (LES) of unknown cause.

! **C/P:**

1. **Vomiting** from the 1st week of life, related to position.
2. **Esophagitis** ⇒ may lead to GIT bleeding & chest pain.
3. **Aspiration pneumonia, recurrent chest infection, chronic cough & wheezing.**
4. **Growth retardation.**
5. **Sudden infant death syndrome** may be a rare complication.

N.B: **Sandifer syndrome:** GERD associated with : severe esophagitis, iron deficiency anemia, vomiting, and abnormal head posturing .

! **Investigations:**

1. **Barium swallow under screen:** shows retrograde filling of dilated esophagus.
2. **Esophageal manometry:** Measures LES pressure (↓↓) + ↓ pH in esophagus.
3. **Continuous esophageal pH monitoring :** using single pH-electrode
GERD is diagnosed If the pH was less than 4 for more than 5% of the monitored time.

! **Treatment:**

1- **Medical TTT:**

- **Feeding** : solids or thickened formulae.
- **Position** : upright position for 30 min. after feeding.
- **Drugs** : Prokinetics e.g. Metochlopramide & Domperidone plus H2 blocker or omeprazole.

2- **Surgical TTT:**

Fundoplication if failed medical TTT with complications.

! **Prognosis:** Very variable and ranges between complete resolution or severe complication. (60% resolve by the age of 2 years).

CONGENITAL HYPERTROPHIC PYLORIC STENOSIS

- **Definition:**

Marked thickening of the pylorus with narrow lumen → vomiting and decrease the nutrients reaching lower GIT.

- **Aetiology:**

- Immaturity of the ganglionic cells within the muscles of the pylorus ⇒ failure of relaxation ⇒ Gradually, contraction and hypertrophy of the circular muscle fibers occur ⇒ Obstruction

- Abnormal muscle innervation, elevated serum levels of prostaglandins, and infant hypergastrinemia have been implicated. Reduced levels of pyloric nitric oxide synthase may play a role.

- **Pathogenesis:**

Progressive pyloric obstruction ⇒ Vomiting ⇒

1. Loss of HCl & K ⇒ Hypokalaemic, Hypochloraemic, Alkalosis
2. Loss of water & Nutrients ⇒ Dehydration

- **Incidence:**

✧ 3/1000 live birth.

✧ More common in male baby, 1st kid of the family 2-3 weeks after birth

✧ Family tendency is present in some cases

- **C/ P:**

1- **Vomiting:** 2-3 weeks after birth shortly after feeding, not bile stained. Early non projectile then becomes projectile. Baby is usually hungry after vomiting.

2- **Constipation:** Small infrequent stool

3- **Dehydration, wt. loss & failure to thrive.**

4- **Jaundice:** Indirect hyperbilirubinemia in 5% of cases (↑ enterohepatic circulation).

5- **Examination:-**

- Palpable mass in the Rt. hypochondrium "Olive tumor ⇒ mobile, not tender"
- Visible peristalsis from Lt. To Rt.

- **Investigations:**

1- **Barium meal shows:**

- Markedly dilated stomach with narrow pyloric canal "shoulder Sign"
- Parallel streaks of barium outlining the pylorus "double tract sign".

2- **Abdominal ultrasound:** Criteria for diagnosis include pyloric thickness >4 mm or an overall pyloric length >14 mm (Sensitivity 95 %).

3- **Metabolic disturbances:** ↑PH, ↓Cl, ↓K, ↓Na.

- **D.D.:** Causes of vomiting in neonates and early infancy.

- **Treatment:**

1- **Surgery:** When established diagnosis.

- Preoperative ⇒ correction of dehydration & electrolytes
- Operative ⇒ pyloromyotomy (Ramstedt's operation)
- Postoperative ⇒ Early feeding (small amount, gradually ↑↑)

II- Medical:

- ✧ Not effective so not recommended except if surgery is contraindicated.
- ✧ Consists of:
 - Feeding → (Small, frequent, thick) Food.
 - Position → (Upright for 1 hour) after feeding.
 - Drugs → (Antispasmodics) 1/2 hour before feeding.

CONGENITAL MEGACOLON "HIRSCHSPRUNG DISEASE"

! Definition:

Narrowing of part of the colon and proximal dilatation without organic obstruction.

! Pathogenesis:

- Absence of ganglionic cells in segment of large intestine usually the rectosegmoid ⇒ failure of relaxation ⇒ functional obstruction
- The proximal colon shows dilatation & becomes full of faeces.

! Incidence:

- Common cause of colonic obstruction
- 1:5000 (Male > Female),
- Common in full term rather than premature babies.
- Common in Down syndrome

! C/P:

- 1- Commonly present since birth by delayed passage of meconium or neonatal constipation
- 2- Some cases remain asymptomatic till present with chronic constipation in infancy or even childhood.
- 3- The disease may be complicated by:
 - Enterocolitis + bloody diarrhea
 - Failure to thrive, and anaemia
 - Toxic symptoms and abdominal distention

! Investigations:

- 1- **Barium enema**: shows dilated colon terminating in funnel shaped manner into narrow segment.
- 2- **Rectal biopsy**: "diagnostic" shows absence of the ganglionic cells in submucosa of biopsy from the narrow segment.

! Treatment:

1- **Medical treatment:**

- ☆ Regular evacuation of the rectum while waiting for operation.
- ☆ Antibiotics in infection.

2- **Surgical treatment:**

- ☆ Always needed (resection-anastomosis).

HEPATOMEGALY

I- Acute liver diseases:

1- Acute hepatitis:

☉ Infectious	☉ Non-Infectious
a- Viruses: ♦ Hepatotropic (ABCDEFGF) ♦ Non (CMV, EBV, yellow fever)	a- Drugs: INH, Paracetamol, Antiepileptics,
b- Bacterial: T B, S, Brucella & septicaemia	b- Metabolic: Wilson, galactosaemia
c- Parasitic: Malaria, Leishmania & β	c- Acute ischaemia

2- Acute congestive heart failure (Rt. Side).

3- Acute stage of veno-occlusive disease.

4- Pyogenic liver abscess.

5- Amoebic liver abscess.

6- Rye syndrome: (Very Rare).

- ☆ Acute encephalopathy with fatty infiltration of the liver
- ☆ Aetiology unknown but related to aspirin intake esp. with viral infection (e.g. chicken pox)
- ☆ Clinically: Vomiting, hepatomegaly without jaundice after recovery from viral illness then delirium, stupor, convulsions and coma.
- ☆ Investigated by ↑ blood ammonia, metabolic acidosis & disturbed LFT.
- ☆ TTT is supportive but prognosis is bad.

II- Chronic liver diseases:

- 1- Chronic hepatitis ⇒ see later
- 2- Chronic hepatic congestion = (Post hepatic causes of portal hypertension)
- 3- Chronic cholestasis. = causes of conjugated hyperbilirubinaemia
- 4- Liver tumours (1ry hepatoma or 2ry).
- 5- Liver cyst: (Congenital e.g. dermoid cyst or acquired e.g. hydatid cyst).
- 6- Metabolic liver diseases: e.g. Amino acid, Fat & CHO storage diseases.

III- Haematological Disorders:

- 1- Chronic hemolytic anaemia.
- 2- Leukaemia and lymphoma.
- 3- Some cases of immune hemolytic anaemia & thrombocytopenia.

IV Collagen Diseases:

- | | | |
|--------|-------------------------|----------------|
| 1- SLE | 2- Rheumatoid arthritis | 3- Amyloidosis |
|--------|-------------------------|----------------|

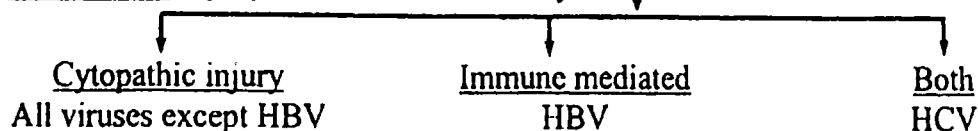
V- Miscellaneous

- | | | |
|----------------|--------------------------------|-------------------|
| 1- Kwashiorkor | 2- Congenital hepatic Fibrosis | 3- Haemosiderosis |
|----------------|--------------------------------|-------------------|

ACUTE VIRAL HEPATITIS

	Hepatitis (A)	Hepatitis (B)	Hepatitis (C)	Hepatitis (D)	Hepatitis (E)
* Cause	Enterovirus (RNA)	Hepadna group (DNA)	Flavi-virus (RNA)	(RNA), non significant except with hepatitis B	Calicivirus (RNA)
* Route	- Faeco-oral	- Parenteral - Perinatal - Sexual - Haemodialysis	- Unknown but may be as Hepatitis B	- As Hepatitis B	- Faeco-oral
* Incubation P.	2-6 weeks	2- 6 months	1-4 months	1-4 months	2-6 weeks
* Epidemiology	Common in school aged children and low socioeconomic $\Rightarrow$ contaminated food	Not common in children but $\uparrow$ risk in: * Chronic blood receivers e.g. hemophiles * Drug abusers	World wide endemic disease common in adults but $\uparrow$ risk as Hepatitis B	The same as Hepatitis B	Rare in children, high mortality in pregnant female (20%)
* Prognosis	Resolution 98%	Fair prognosis	Fair	Fair	Resolution
* Ch. Hepatitis	--	May occur	May occur	May occur	--
* Carrier	--	May occur	May occur	May occur	--
* Cirrhosis	--	May occur	May occur	May occur	--
* Carcinoma	--	May occur	May occur	May occur	--
* Fulminant hepatic failure	Rare	Common	Common	Common	Rare
* Prevention	* Health education * Food Hygeine * Vaccine is present	* Health education * Blood analysis * Vaccine is present	* Health education * Blood analysis * No vaccine	* Health education * Blood analysis * Vaccine for Hepatitis B ¹¹	* Health education * No Role * No vaccine
* TTT	* Rest * $\uparrow$ CHO diet + vitamins * Avoid hepatotoxic drugs	* Supportive ttt as Hepatitis A * Management of complications	* As Hepatitis B	* As Hepatitis B	* Supportive

• **Pathology:** Injury of the liver cells may be: $\downarrow$



• **Clinical picture of acute viral hepatitis:**

Manifestations pass into 3 phases

1- **Pre-icteric** (2-4 weeks)

- ☆ Fever, severe anorexia, headache & malaise
- ☆ Nausea, vomiting, abdominal pain

2- **Icteric phase** (2-4 weeks)

- ☆ Jaundice with dark urine & clay coloured stool
- ☆ Fever, nausea,.... All disappear by the appearance of jaundice
- ☆ Tender hepatomegaly $\pm$ splenomegaly (25% of cases)

3- **Convalescent phase**

- ☆ Complete resolution especially hepatitis A & E.
- ☆ Sometimes pass to chronicity or fulminant hepatic failure esp. in other types

- **N.B.** ⇒ in viral hepatitis esp. B, C & D the acute manifestations are frequently absent (i.e. A lot of cases pass unnoticed & the patient may present with complications), so most (B, C, D) acute hepatitis are asymptomatic (even without jaundice).

• **Investigations of acute viral hepatitis**

1- **Urine** ⇒ Dark colour with ↑ cholebilirubin and bile salts.

2- **Stool** ⇒ Pale colour with ↓ stercobilinogen

3- **Liver function tests** ⇒

- **Serum bilirubin level** → Moderate ↑ (Conjugated or mixed)
- **ALT & AST** → Highly elevated up to thousands (ALT is more specific than AST).
- **Alkaline phosphatase** → mild elevated.
- **Serum proteins & PT** → usually normal (acute disease)

4- **Serology:**

• **Hepatitis A infection:** (Not needed)

- ⇒ Antibodies
 - IgM anti-HAV (Early) → recent infection
 - IgG anti-HAV (Late) → previous infection
- ⇒ Antigen → Viral isolation from stool esp. in pre-icteric phase

• **Hepatitis C infection:**

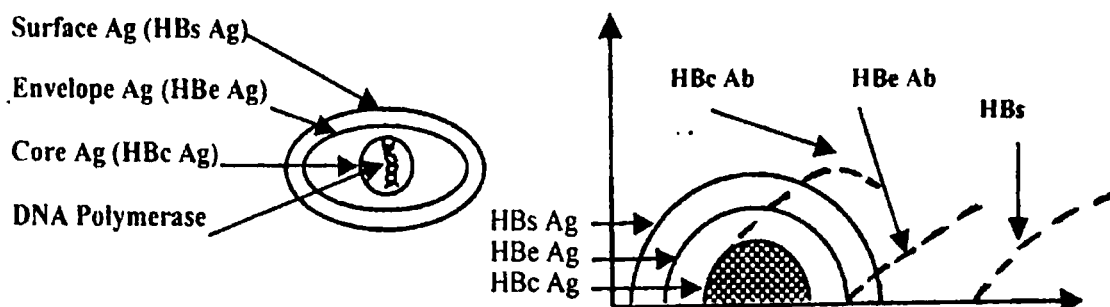
- ⇒ Antibodies → Anti-HCV (IgG, IgM) ⇒ not accurate due to false + ve results.
- ⇒ Antigen → Identification of HCV RNA by (PCR) ⇒ Reliable.

• **Hepatitis D infection:** • As Hepatitis C (Anti-HDV Ab & Ag).
N.B. (Hepatitis B must be proven first)

• **Hepatitis E infection:** • As Hepatitis C (Anti-HEV Ab & Ag).

• **Hepatitis B infection:** Very important

Antigen	Significant	Antibody	Significant
HBs Ag	⇒ Infection "Acute or chr."	HBs Ab	⇒ Recovery or immunity
HBe Ag	⇒ High infectivity	HBe Ab	⇒ End of viral replication (low infectivity)
HBc Ag	⇒ Not present in serum "only in hepatocytes"	HBcAb IgG	⇒ Acute or chr. infection
DNA polymerase	⇒ Infection "Acute or chr."	HBc Ab IgM	⇒ The single most reliable marker for HBV infection



CHRONIC HEPATITIS

- **Definition:** Continuing hepatic inflammatory process manifested by elevated serum transaminases (ALT & AST). Old definition determined the duration of liver disease to be at least 6 months. Now current criteria emphasize that in the presence of severe liver disease or physical signs of chronic liver disease, a shorter time may be employed.
- **Causes:**
 - 1- **Autoimmune hepatitis:** (the commonest cause) due to self antibodies against hepatocytes.
 - 2- **Persistent viral infection:** (B, C or D + B)
 - 3- **Miscellaneous (rare):**
 - Drug induced.
 - Metabolic disorders e.g. Galactosemia, Wilson disease.
- **Pathology:**

Varies according to aetiology and comprises affection of the hepatocytes, portal tracts and central area involvement. Staging system was generated (METAVIR) to enable the clinician and pathologist to decide regarding the therapeutic plan. The old terms of chronic active and chronic persistent hepatitis has been abandoned.
- **C/P:** Different presentations:
 - 1- May be **asymptomatic** (accidentally discovered).
 - 2- **Non specific manifestations** (fatigue, malaise, anorexia ± tenderness on Rt. hypochondrium).
 - 3- **Extrahepatic manifestations:** Arthritis, nephritis, thyroiditis, skin rash, Coomb's +ve hemolytic anaemia, aplastic anaemia, pleurisy & pericarditis.
 - 4- Rarely, the patient may present with **picture simulating acute hepatitis**.
 - 5- Some patients may present with **complications** (Cirrhosis / Carcinoma / FHF).
- **Investigations:**
 - 1- **LFT:**
 - ALT & AST (mild to moderate ↑).
 - Bilirubin: slight ↑ (2 – 10 mg/dl)
 - Alkaline phosphatase, PT & albumin → may be impaired.
 - 2- **Features of cause:**
 - If autoimmune: - ↓ complement
 - Presence of antibodies against liver cells e.g. LSP, LKM.
 - If post-viral: - Hepatitis markers according to the cause (see before)
 - If metabolic: - Investigations for the cause.
- **Treatment:**
 - 1- Supportive measures / ttt of complications.
 - 2- Specific treatment:
 - For autoimmune → corticosteroids 2mg/kg/day then gradual ↓ when transaminases return to normal, if no response to steroids azathioprine can be added.
 - For post viral → interferon - α IM 3 times /week
 - 3- Liver transplantation in end stage LCF.
- **Prognosis:**
 - Response to ttt occurs in 50% of cases, however, most of cases shows relapse after stoppage of ttt (steroids or interferon).
 - Spontaneous recovery may occur in few cases.

PORTAL HYPERTENSION

* Definition:

↑↑ portal vein pressure > 10 mmHg (Normally 7 mmHg).

* Causes of portal hypertension:

1- Post hepatic causes:

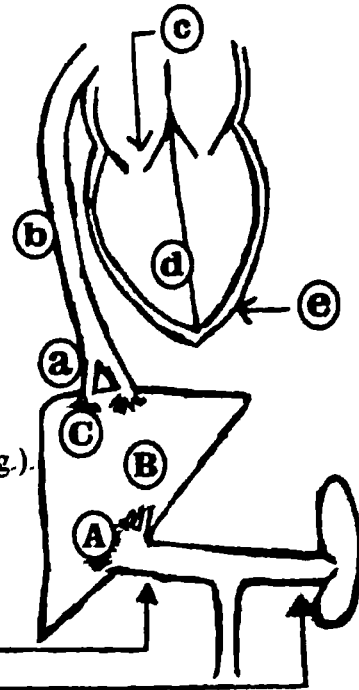
- a- Hepatic vein obstruction (Budd-chiari syndrome).
- b- Inferior vena cava obstruction.
- c- Tricusped regurge.
- d- Congestive heart failure.
- e- Pericardial effusion and constrictive pericarditis.

2- Hepatic causes:

- A- Pre sinusoidal: Portal tract fibrosis or infiltration (Malig.).
- B- Sinusoidal: Liver cirrhosis.
- C- Post sinusoidal: Veno-occlusive dis. of the liver.

3- Pre hepatic causes:

- ◇ Obstruction of portal vein (1ry or 2ry to sepsis).
- ◇ Obstruction of splenic vein (1ry or 2ry).



* Manifestations:

1- Collateral circulation opening:

(opening of porto-systemic shunts to drain portal blood)

- ◇ GIT bleeding ◇ Caput medusa ◇ Venous hum.

2- Ascitis.

3- Splenomegaly.

- 4- Liver → Pre Hepatic → Normal size.
- Hepatic → Cirrhotic = shrinkage.
- Post hepatic → Enlarged.

* Investigations:

- 1- Upper endoscopy: to detect bleeding varices ± TTT.
- 2- Abdominal sonar: to detect liver/spleen and minimal ascitis.
- 3- Measurement of portal vein pressure.
- 4- Angiography of portal system.
- 5- Investigations for the cause.

* Treatment:

- 1- Treatment of the cause if possible
- 2- Prevention of bleeding by β blockers (propranolol) → ↓ portal blood pressure.
- 3- TTT of bleeding varices (see page 247).

LIVER CIRRHOSIS

* Definition:

Chronic diffuse liver disease chch. by:

- ☆ Degeneration and necrosis of liver cells
- ☆ Regenerating nodules
- ☆ Loss of hepatic architecture (DD from fibrosis e.g. Bilharsiasis in which no parenchymal damage occurs)

* Aetiology:

- 1- Post hepatic cirrhosis: After chronic HBV or HCV (Commonest)
- 2- Alcoholic "nutritional" cirrhosis.
- 3- Biliary cirrhosis:
 - ♦ 1ry (unknown cause) ♦ 2ry to obstruction to bile flow
- 4- Cardiac (Congestive) cirrhosis: Chronic hepatic congestion "as post hepatic causes of portal hypertension".
- 5- Mixed β cirrhosis = β + viral hepatitis
- 6- Metabolic cirrhosis: Wilson, Haemochromatosis,

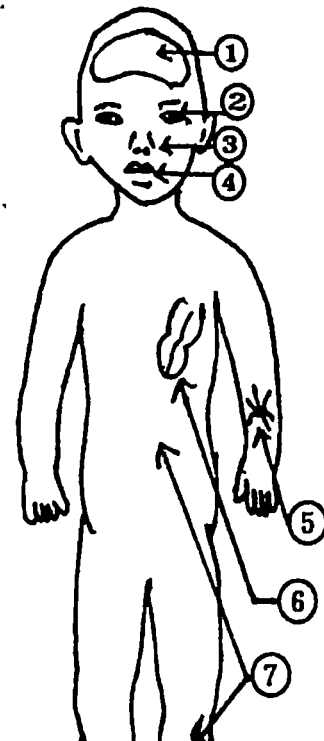
* Clinical manifestations:

I- Compensated cirrhosis:

- ☆ Non specific manifestations (Anorexia, fatigue,...)
- ☆ Manifestations of the cause

II- Decompensated cirrhosis: Manifestations of liver cell

- 1- Hepatic encephalopathy.
(Drowsiness, Flappy tremors → coma)
- 2- Jaundice
- 3- Foetor hepaticus "Fruity apple odour from the mouth"
- 4- GIT bleeding "e.g. Hematemesis, melaena"
- 5- Cutaneous manifestations "spider naevi, palmer erythema"
- 6- Circulatory manifestations (hyperdynamic circulation or ↓BP).
- 7- Ascitis & peripheral oedema (Due to ↓ protein & portal hypertension)
- 8- General deterioration of health



* Investigations:

- 1- LFT: (Bilirubin, ALT, AST, PT, Alk. Phosphatase, Albumin)
Abnormal if decompensated / Normal or slightly abnormal if compensated.
- 2- Imaging: Sonar abdomen, CT, MRI, GIT endoscopy
- 3- Liver biopsy: Diagnostic ⇒ contra-indicated in ascitis & prolonged P.T.
- 4- For the cause: e.g. viral markers.

* Complications (3H)

- 1- portal Hypertension 2- Hepatorenal syndrome 3- Hepatoma

* Treatment:

- 1- Supportive care.
- 2- TTT of the cause.
- 3- Antifibrotic drugs (colchicine)
- 4- In (LCF) → Liver transplantation.

ASCITIS

* Types of ascitic fluid:

	<i>chch</i>	<i>causes</i>
1- <u>Transudate</u>	- Clear fluid - ↓ Sp.gr. (< 1015) - ↓ Ptn. (< 3gm%) - Few cells - No organisms	• Causes of generalized oedema with ascitis • Meig's syndrome • Polyserositis
2- <u>Exudate</u>	- Turbid fluid - ↑ Sp.gr. (> 1015) - ↑ Ptn. (>3gm%) - Many cells - Organisms may present	• Peritonitis: - Bacterial - Tuberculous - Post traumatic
3- <u>Haemorrhagic</u>	- Bloody with RBC's	• Trauma • Tumours • T.B.
4- <u>Chylous</u>	- Milky white fluid	• Obstruction or trauma to the thoracic duct
5- <u>Others</u> [Bilous / Urinary]		→ due to trauma

* D.D. of ascitis (abdominal distention):

- ♦ Flatulance (Gases)
- ♦ Fat (obesity)
- ♦ Foreign mass (e.g tumours & cysts)
- ♦ Full bladder
- ♦ Fetus (Pregnancy)
- ♦ Fluid = Ascitis

GIT BLEEDING

Causes:

1- Upper GIT bleeding:

- * Bleeding originates above the ligament of treitz in the form of hematemesis or melena (dark tarry stool).
- * Important causes:
 - ♦ Esophageal → trauma, tumours, GERD and esophageal varices.
 - ♦ Stomach → stress ulcer, peptic ulcer.
 - ♦ Intestine → duodenal ulcer.

2- Lower GIT bleeding:

- * Bleeding originates below the ligament of treitz in the form of bleeding/rectum..
- * Important causes:
 - ♦ Intestinal obstruction (volvulus, intussusception)
 - ♦ Intestinal polyps
 - ♦ Anal fissures
 - ♦ Inflammatory bowel diseases.
 - ♦ GE
 - ♦ Rare causes (FB, sexual abuse, intestinal telangiectasia)

3- Hemorrhagic blood diseases:

- * Either upper or lower GIT bleeding.
- * Important causes:
 - ♦ Platelet defect
 - ♦ Vascular defect
 - ♦ Coagulation defect

Management:

I- Emergency measures:

- ♦ Admission to hospital.
- ♦ Rapid venous access.
- ♦ Monitoring of pulse / BP and amount of bleeding.
- ♦ Blood transfusion (after determination of Hb%).
- ♦ Vit. K.
- ♦ Antacids (e.g. Aluminum hydroxide gel)

II- Diagnosis of the cause:

* History:

- ♦ Dark stool suggests melena while fresh red blood suggests bleeding/rectum.
- ♦ Of preceding diarrhea → GE.
- ♦ Of liver disease → esophageal varices.
- ♦ Of bleeding disorder.

* Examination:

- ♦ Hepatosplenomegaly and ascitis → esophageal varices.
- ♦ P/R → for piles or anal fissure.
- ♦ Purpura and pallor → leukaemia or aplastic anaemia.
- ♦ Abdominal distention → intestinal obstruction.
- ♦ Frequent regurgitation → GERD.

* Investigations:

- ♦ Endoscopy → for esophageal varices and peptic ulcer.
- ♦ X-ray → for intestinal obstruction.
- ♦ Manometry studies → for GERD.
- ♦ Investigations for bleeding disorders e.g. bleeding time, clotting time,
- ♦ Stool analysis → for GE.

III- Treatment of the cause:

- ♦ Esophageal varices →

1- <u>Drugs:</u> e.g. vasopressin → ↓ portal pressure. 2- <u>Sungstaken Blackmore tube:</u> Compression on the bleeding varices. 3- <u>Endoscopy:</u> Injecting sclerotic material (obliterate the varices). 4- <u>Emergency shunt:</u> In unresponding severe bleeding.	* <u>Measures to avoid hepatic encephalopathy.</u> - Protein restriction. - Neomycin syrup. - Lactulose enema.
--	---

- ♦ Bleeding disorders → see before (blood).
- ♦ GERD → see before (GIT).
- ♦ Peptic ulcer → antacids + H₂ receptor blockers.
- ♦ Intestinal obstruction, polyps, piles → surgery.

MISCELLANEOUS SUBJECTS

● **Veno- occlusive disease (VOD):**

- ♦ **Def.** Intrahepatic obstruction of the hepatic veins.
- ♦ **Aet.** Unknown, may be toxic injury to wall of hepatic veins by herbal teas.
- ♦ **C/P**
 - 1- Acute stage = Portal hypertension, hepatomegaly & No splenomegaly.
 - 2- Subacute stage = Portal hypertension, hepatomegaly & splenomegaly
 - 3- Chronic stage = Portal hypertension, shrinkun liver & splenomegaly.
- ♦ **Invest.** 1- As portal hypertension 2- Liver biopsy (Diagnostic)
- ♦ **TTT.** 1- Symptomatic 2- In severe cases liver transplantation

● **Budd-chiari syndrome:**

- ♦ **Def.** Post hepatic obstruction of the main hepatic veins (extra hepatic).
- ♦ **Aet.**
 - 1- 1ry (idiopathic): Most cases.
 - 2- 2ry (Trauma, polycythaemia, infection, malignancy).
- ♦ **C/P**
 - 1- Acute stage: Abd pain, vomiting, hepatomegaly
 - 2- Chronic stage: Portal hypertension + congested liver
- ♦ **Invest:** As portal hypertension
- ♦ **TTT:** 1- Symptomatic 2- In severe cases liver transplantation

● **Wilson disease:**

- ♦ **Aet :** AR disorder chch by defective ceruloplasmin which is Ptn. necessary for cupper transport
- ♦ **Pathogenesis:** Defective Cu transport → ↑ free Cu in blood → deposition on various organs.
- ♦ **C/P:** according to the affected organ:
 - ① Liver → Hepatitis & cirrhosis.
 - ② Basal ganglia → Behavioral & speech disorders.
 - ③ Cornea → Kayser Flisher ring.
 - ④ Kidney → Fanconi like syndrome.
 - ⑤ RBC's → Hemolysis
- ♦ **Invest.**
 - ① ↓ serum ceruloplasmin.
 - ② increased urinary Cu before and after D-penicillamine dose.
 - ③ ↑ Cu content in liver biopsy.
 - ④ screen all the siblings around the index case for possible cases.
 - ⑤ Genetic study for the molecular variant.
- ♦ **TTT:**
 - ① restrict cupper in the diet i.e. chocolate, shell fish and liver.
 - ② Cupper chelating agents (D-penicillamine)
 - ③ In severe cases liver transplantation

CHAPTER (VI)

CHEST

Anatomical considerations

Anatomy of chest of neonates and infants differ from older children & adults in the following:

- 1- Horizontal ribs & soft chest wall leads to marked chest wall retraction during respiratory distress than older individuals.
- 2- Narrow airways esp. upper leads to easily obstructed lumen by mucus, FB or inflammation.
- 3- Thin chest wall leads to hyperresonant note and loud breath sounds.
- 4- Smooth muscles are present since birth, so, bronchospasm may occur early in life.
- 5- Respiratory pattern is mainly abdominal during the 1st 2 years of life.

I- UPPER RESPIRATORY DISEASES**Acute Pharyngitis**☆ **Def:**

Acute infection in the form of tonsillitis, pharyngitis or tonsillopharyngitis caused by viral infection or bacteria (especially group A β -hemolytic streptococci).

☆ **C/P:**

- 1- **General manifestations:** Fever, headache, malaise, mild anorexia $\pm$ vomiting.
- 2- **Sore throat:** Accompanied with difficult swallowing, tonsillar enlargement and cervical lymphadenopathy.

☆ **Investigations:**

Throat swab is occasionally needed to prove streptococcal infection.

☆ **Complications:**

The same as scarlet fever + mesenteric adenitis $\rightarrow$ abdominal pain.

☆ **Treatment:**

- 1- **Symptomatic treatment:** for fever, pain,
- 2- **Penicillin** for 10 days in strept infection (in penicillin allergy $\Rightarrow$ erythromycine).
- 3- **Tonsillectomy** is indicated if:
 - Frequent tonsillitis resulting in prolonged absence from school
 - Peri-tonsillar abscess (Quinzy).
 - Suspected malignancy in the tonsils.
 - Resistant diphtheria carrier.
 - Obstructive sleep apnea (adeno-tonsillectomy is indicated).

Acute Otitis Media

☆ **Pathogenesis:**

⊛ 2 factors are co-operating:

- 1- **Eustachian tube obstruction:** By oedema and inflammation 2ry to viral URTI or large adenoids.
- 2- **Bacterial invasion:** Commonly H. influenza , pneumococci and moraxella catarrhalis.

☆ **C/P:**

- ⊛ Fever, irritability and rubbing of the ear.
- ⊛ Severe pain which relieves when perforation of the drum occurs with passage of pus from the external auditory meatus.
- ⊛ Otoscopic exam. shows bulging of the drum (early) or perforation (late).

☆ **Treatment:**

- 1- **Symptomatic:** For pain, fever,
- 2- **Antibiotics:**
 - amoxicillin- clavulanic acid , oral azithromycin or ceftriaxone injection.
- 3- **Tube drainage:** In secretory OM "Grommet's tube"

Sinusitis

Acute infection of the nasal sinuses caused by viral or bacteria infection.

☆ **Etiology:**

Streptococcal pneumoniae (30%), H. influenza (20%), Maroxella catarrhalis 20%.

☆ **Clinical Picture:**

- 1- General manifestations: fever, headache, nasal congestion, nasal discharge ,cough
- 2- Less common: bad breath (halitosis), decreased smell and periorbital edema.

☆ **Investigations:**

- Sinus aspirate culture.
- Radiographic studies (plain X ray and CT scans).

☆ **Treatment:**

- 1- Symptomatic treatment.
- 2- Antibiotic (e.g. Amoxycillin /clavulanic acid).

Stridor

☆ Def.:

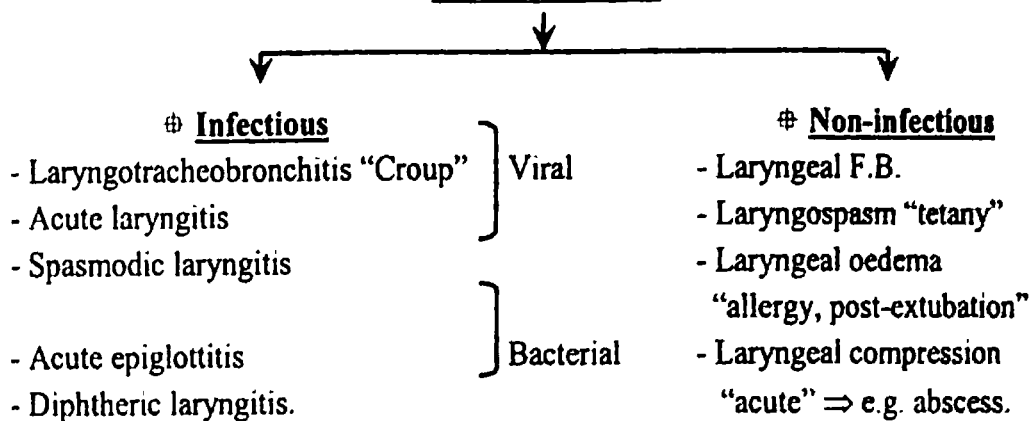
Continuos inspiratory harsh sound produced by partial obstruction in upper airways (larynx and trachea).

☆ Clinical grades of stridor:

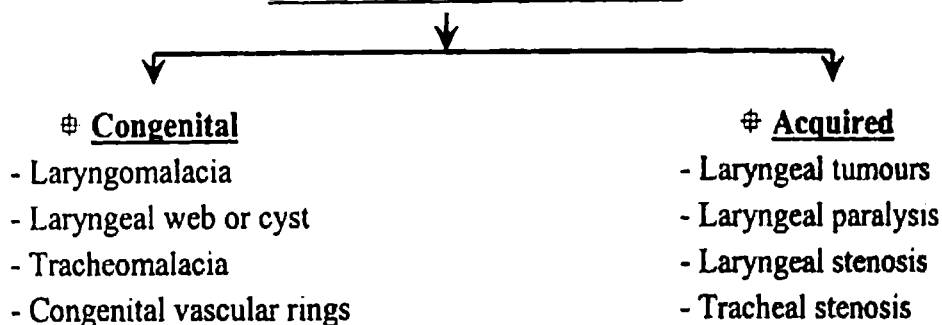
- ◆ Grade I → stridor on exertion.
- ◆ Grade II → stridor at rest.
- ◆ Grade III → stridor with intercostal retraction
- ◆ Grade IV → stridor with cyanosis.

☆ Causes of stridor:

1- Acute stridor



2- Chronic "Persistent" stridor



* Acute Infectious Stridor *

	1- Laryngo-tracheo – bronchitis	2- Acute laryngitis	3- Spasmodic laryngitis
• <u>Age</u>	* 6 months – 6 years	* 1-3 years	* 1-3 years
• <u>Cause</u>	* Viral esp. para-influenza virus type 1, 3 may be RSV or adenovirus.	* Viral	* Viral but may be allergy or psychogenic
• <u>C/P</u>	* Preceded by URTI * Moderate fever * Both insp. and exp. stridor. moderate – severe * Croupy cough and hoarseness of voice * Manifestations of respiratory distress and chest signs may occur.	* Preceded by URTI * Mild fever * Insp. stridor mild – moderate * Croupy cough and hoarseness of voice. * No respiratory distress except in young children	* Sudden esp. at night * No fever * Insp. stridor mild – moderate * Croupy cough and hoarseness of voice. * Respiratory distress may occur * recurrence is common
• <u>TTT</u>	1- O ₂ , steam inhalation or nebulized adrenaline. 2- Adequate hydration "I.V. fluids may be needed". 3- Corticosteroids (controversial) 4- Tracheostomy may be done in severe upper respiratory obstruction		

4- Acute Epiglottitis

☆ Aetiology:

Infection of epiglottis and subglottic areas by H. influenza type-B. Rarely other bacteria may be involved (e.g. staph, strept. or pneumococci)

☆ C/P:

- ◆ Affected child usually aged 2-7 years.
- ◆ Sudden onset of high fever, toxemia and respiratory distress.
- ◆ The child usually adopt upright position with drooling of saliva (due to dysphagia), neck extension and severe exhaustion.
- ◆ No cough and stridor is usually mild.
- ◆ Any stressful procedures (e.g. injections, maneuvers, throat exam) may precipitate complete upper airway obstruction.

☆ Treatment:

- 1- Admit to ICU and avoid any procedure that may precipitate obstruction.
 - 2- X-ray lateral area of the neck may show swollen epiglottis "thumb sign", but not done except in presence of medical person experienced in intubation.
- N.B.* ⇒ Some centers recommend routine endotracheal intubation for 2-3 days.
- 3- O₂ therapy and fluids.
 - 4- Antibiotics → I V 3rd generation cephalosporins (co-trimoxazole is less effective).

☆ Prognosis:

- ◆ Very serious condition with high mortality.
- ◆ The incidence has been declined in a lot of developed countries due to routine immunization against H. influenza type B (Hib v

II- LOWER RESPIRATORY DISEASES

Examination of important chest diseases

	Pneumonia	Broncho-pneumonia	Collapse	Pleural effusion	Pneumo-thorax	Hydropneumothorax
• <u>Inspection</u>						
- Movement	↓↓	↓↓ (? Bil.)	↓↓	↓↓	↓↓	↓↓
- Shape	Normal	Normal	Retraction	Bulge	Bulge	Bulge
• <u>Palpation</u>						
- Tracheal shift	Central	Central	To same side	To opposite side	To opposite side	To opposite side
- TVF	↑↑	± normal	↓↓	↓↓	↓↓	↓↓
• <u>Percussion</u>						
- Note	Impaired	± impaired	Dull	Dull	Hyperresonance	Shifting dullness
- Topography	Lobar	Bilateral	Lobar	Rising to axilla	Allover the side	Transverse upper border
• <u>Auscultation</u>						
- Breath sounds	Bronchial	Vesicular ± bronchial	Diminished vesicular (except massive)	Diminished vesicular (except massive)	Diminished vesicular	Diminished vesicular
- Adventitious sounds	No ± crepit	Bil.crepit ± wheezes	No	No	No	No
- Vocal resonance	↑↑	± normal	↓↓	↓↓	↓↓	↓↓
• <u>Special signs</u>	Bronchophony	No	No	Aegophony	Coin test	Succession splash

Pneumonia

☆ **Def:** Inflammation of the lung parenchyma.

☆ **Classification:**

I- Aetiological:

- 1- **Bacterial:** Pneumococci, staph, strept, H. influenza & klebsiella.
- 2- **Mycoplasma:** (1ry atypical pneumonia).
- 3- **Viral:** Respiratory syncytial virus, adenovirus, influenza, parainfluenza & measles.
- 4- **Fungal:** Aspergillosis and histoplasmosis.
- 5- **Protozoal:** Pneumocystis carinii.
- 6- **Aspiration:** Food, kerosene, oils and milk.
- 7- **Allergic:** Löffler's pneumonia → Hypersensitivity to worms or larva migrans.
- 8- **Hypostatic:** In prolonged recumbency.

II- Anatomical:

- 1- **Lobar pneumonia:** Unilateral consolidation in one or more lobes
"usually bacterial in origin".
- 2- **Bronchopneumonia "Lobular pneum":** Bilateral small patchy consolidation
along the distribution of the bronchial tree "may be viral or bacterial".
- 3- **Interstitial pneumonia:** Bilateral small foci of consolidation along the
distribution of the small bronchioles "usually viral in origin".

☆ **C/P:**

1- Symptoms.

- ✧ **Onset:** Acute (esp. in bacterial) or gradual.
- ✧ **General:** Fever, anorexia, malaise and fatigue.
General condition is worse in bronchopneumonia than lobar pneumonia.
- ✧ **Chest:** - Cough (dry then productive) - Dyspnea - Grunting

2- Examination:

✧ **Signs of respiratory distress:**

- Grade I "tachypnea and working alae nasi"
- Grade II "Retraction → inter-costal and sub-costal".
- Grade III "Grunting"
- Grade IV "Cyanosis"

✧ **Chest examination:**

- Lobar pneumonia
 - Bronchopneumonia
- } See before
- Interstitial pneumonia → chest signs are usually minimal or absent with tendency for prolonged expiration and expiratory wheezing.

☆ Investigations:

1- Chest X-ray:

- ✧ **Lobar pneumonia:** Homogenous opacity involving one or more of lung lobes.
- ✧ **Bronchopneumonia:** Scattered bilateral opacities in both lungs.
- ✧ **Interstitial pneumonia:** Scattered bilateral perihilar pulmonary infiltrate or reticulonodular infiltrate.

☞ **N.B.:** X-ray may show complicated pneumonia:

e.g. cavities, pneumatocele, pleural effusion or collapsed areas.

☞ **N.B.:** Chest US can detect small amount of pleural effusion.

2- Investigations to identify the cause:

- ✧ **Blood** → Leukocytosis, ↑ESR and ↑CRP are more suggestive of bacterial than viral pneumonia.
- ✧ ↑ASO titre → streptococcal pneumonia.
- ✧ **Cold agglutinins in blood** → mycoplasma pneumonia.
- ✧ **Culture and sensitivity** → of sputum, pleural fluid or blood for bacterial pneumonia.
- ✧ **Viral isolation or serology** → for viral pneumonia.

☆ Complications:

- 1- **Lung:** Abscess, collapse and pneumatocele.
- 2- **Pleural:** Pleurisy, effusion and empyema.
- 3- **C.V.S.:** Pericarditis and H.F.
- 4- **Toxic:** Sepsis, meningismus, SIADH.

☆ Treatment of pneumonia:

- 1- **General:** Rest-adequate hydration – light diet
(If severe RD → hospitalization, O₂ & IV fluids).
- 2- **Symptomatic:** For: fever – cough – chest pain.
- 3- **Antibiotics “If bacterial”:**
 - * According to culture and sensitivity if available.
 - * Clinical features and X-ray may suggest the cause (see D.D.).
 - * If the causative bacteria is not known combination antibiotic ttt is indicated.
- 4- **Antiviral:** If viral pneumonia occurs in immunocompromized child.
- 5- **Treatment of complications:**
 - * TTT of heart failure.
 - * Aspiration of non resolved effusion and intercostal tube for empyema.

☆ **D.D.:**

Pneumonia may differ in presentations according to the causative agent that may affect the treatment.

1- **Bacterial Pneumonia:**

	Pneumococcal	Streptococcal	Staphylococcal	H.influenza	Klebsiella
Incidence	- The most common bacterial pneumonia - Age (<4 yrs)	- Peak age 3-5 yrs	- Common in infancy (< 1yr)	- Peak age (< 3 yrs)	- Mainly in debilitated child
C/P	- Moderate - Commonly complicated by meningism	- Moderate - High fever and chills are common	- Severe - High fever and ↑ incidence of complications	- Insidious onset and prolonged course over weeks.	- Sudden onset, progressive and ↑↑ fatality
X-ray	- Usually lobar may be broncho in young infants ± pleural effusion	- Usually broncho. ± pleural effusion	- Broncho but may be lobar ± pneumatocele or effusion	- Lobar but may be broncho. If lobar usually more than one lobe are affected	- Lobar with complications (abscess, cavitation, ...)
Drug of Choice	- Penicillin, vancomycin if resistant	- Penicillin	- Cloxacillin or vancomycin	- 3rd generation cephalosporins	- amikacin or meropenem.

2- **Mycoplasma pneumonia:** "1ry atypical pneumonia"

- ✧ Incidence: The most common form of pneumonia in school aged children
- ✧ C/P:
 - * Severe spasmodic cough without significant R.D.
 - * Minimal chest signs (may appear later in the disease).
- ✧ X-ray chest:
 - * Perihilar lower lobes infiltrate (resembling interstitial pneumonia).
 - * Some times lobar consolidation ± effusion
- ✧ Cold agglutinins in the blood may support the diagnosis.
- ✧ Complications include autoimmune hemolytic anemia, encephalitis and Steven-Johnson syndrome.
- ✧ Treatment: Erythromycin or azithromycin.

3- **Viral pneumonia:**

- ✧ Incidence: The commonest cause in pre-school children.
- ✧ C/P:
 - * History of preceding URTI
 - * Mild fever and good general condition.
 - * Few physical signs (± crepitations or wheezes).
- ✧ X-ray chest: Bronchopneumonia or interstitial pneumonia.
- ✧ TTT: Supportive (Antiviral in immunocompromised child)

Acute Bronchiolitis

☆ **Def:** Acute inflammatory obstruction of the bronchioles "small airways"

☆ **Aetiology:**

- 1- Respiratory syncytial virus (60% of cases).
- 2- Others: para influenza virus, adenovirus and mycoplasma.

☆ **Pathogenesis:**

- Small bronchioles are invaded by the virus → inflammation and oedema → bronchiolar obstruction.
- Bronchiolar obstruction → hyperinflation, prolonged expiration & respiratory distress.
- Defective gas exchange (severe cases) → hypoxia.

☆ **Incidence:**

- Age: Not occur after 2 years (peak age around 6 months).
- Sex: Common in male.
- Season: Common in winter and spring.

☆ **C/P:**

⊗ **Symptoms:**

- 1- Onset with URTI "Rhinitis, mild fever" for few days.
- 2- Gradual appearance of respiratory manifestations:
 - Cough.
 - Dyspnea (manifested by feeding difficulty)
 - Wheezy chest.
- 3- Associated severe irritability and crying.

⊗ **Signs:**

- 1- General signs of respiratory distress of variable severity.
Dehydration may present in severe cases.
- 2- Chest examination:
 - Inspection: Hyperinflation and prolonged expiration (Bilateral).
 - Palpation: Central trachea and ↓ TVF.
 - Percussion: Bilateral hyperresonance.
 - Auscultation:
 - Diminished vesicular breathing with prolonged expiration
 - Wheezes ± crepitations.

N.B. Liver & spleen may be ptosed and felt abdominally (due to chest hyperinflation)

☆ **Complications:**

- 1- Respiratory failure.
- 2- Heart failure (rare)
- 3- Dehydration
- 4- 2ry bacterial pneumonia
- 5- Recurrence: (recurrent bronchiolitis may indicate that the infant will be asthmatic & some authors suggest that the 3rd attack of bronchiolitis is considered asthma).

☆ **Investigations:**

Diagnosis of bronchiolitis is mainly clinical and investigations are of little value:

- 1- X-ray chest: Hyperinflated lung $\pm$ areas of collapse.
- 2- Acute phase reactants (ESR, CRP,): usually normal or mildly elevated.
- 3- In severe cases identification of respiratory syncytial virus by immunofluorescence of nasopharyngeal swab.

☆ **D.D.:**

- 1- From other causes of wheezy chest esp. asthma.
- 2- From other causes of R.D. esp. pneumonia.

☆ **Treatment:**

- 1- **In mild attack without RD** $\rightarrow$ follow up.

- 2- **In severe attack or dehydration:**

- Hospitalization, humidified O₂ & IV fluids.
- Adrenaline, 5 ml of 1:1000 inhalation by nebulizer is safe and effective.
- Bronchodilators and cortecosteroids $\rightarrow$ controversial.
- TTT of complications (NaHCO₃ for acidosis, mechanical ventilation for respiratory failure and digitalis for H.F).

- 3- **In high risk infants:** (CHD, immuno-compromized, severely ill, BPD)

- Antiviral (Ribavirin) $\rightarrow$ by continuous inhalation.

***for prevention of severe disease.**

- Respiratory syncytial virus immunoglobulins
- Palivizumab monoclonal antibody directed against an epitope in the F protein of RSV.

☆ **Prognosis:**

- The first 48 hours of the illness are the most critical, usually followed by gradual improvement.
- Mortality rate about 1% (due to respiratory failure, heart failure or severe dehydration)

Bronchial Asthma

☆ **Def:**

Chronic inflammatory disorder of the airways with cellular infiltration and:

- Hyper-reactivity of airways

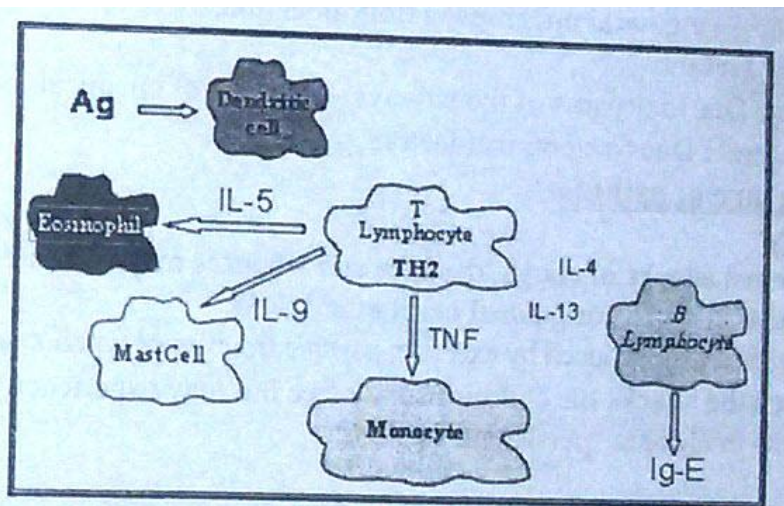
- Hyper-reactivity of airways to a variety of stimuli.
- High degree of reversibility of the obstructive process either spontaneously or with treatment

☆ Epidemiology:

- 5 -15 % of children may suffer asthmatic attacks during any age, from them 1/3 rd will carry their illness into adult life.
- 30% of asthmatics are symptomatic by one year of age and 80-90% by 4-5 years.
- Family history is present in a lot of cases.
- Other features of atopy may present in the same child e.g. contact dermatitis and nasal allergy.

☆ Pathogenesis:

- Immune System Development is Key to Development of Allergy and Asthma
- Asthma is characterized by a TH2 immune phenotype
- 80-90% of all childhood asthma is associated with atopy skin test reactivity, increased total & specific IgE
- Allergic inflammation mediated by TH2 cytokines

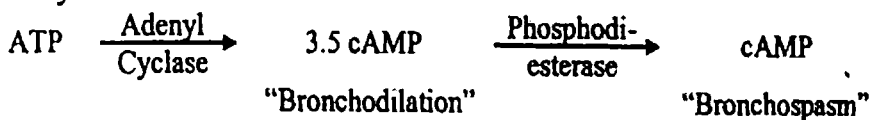


I- A lot of mechanisms are suggested to induce asthma:

1- Autonomic mechanism:

- Parasympathetic predominance and ↓ sympathetic drive.

* Normally



- * Factors which ↑ adenylyl cyclase e.g. catecholamines ⇒ bronchodilatation.
- * Factors which ↑ phosphodiesterase e.g. acetyl choline ⇒ bronchospasm.

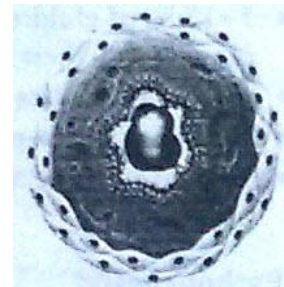
2- Atopy "type I hypersensitivity":

- * Exposure to certain allergens $\rightarrow$ $\uparrow$ IgE production which attach to mast cells in the bronchial wall.
- * On re-exposure to the same allergen $\rightarrow$ allergen/IgE interaction $\rightarrow$ rupture of mast cells $\rightarrow$ liberation of certain mediators (Leukotriens, PG, histamine) which induce bronchospasm and other bronchial changes.

3- Remodeling of the air ways due to persistent inflammation with submucosal collagen deposition and muscular hypertrophy.

II- Changes in bronchial asthma:

- 1- • Lumen $\rightarrow$ mucus excess
+ inflam. debris
• Muscular layer $\rightarrow$ spasm
- * Narrow air ways
esp. in expiration



2- Narrow air ways will lead to:

- Air trapping $\rightarrow$ Hyperinflated lung + Resp. distress.
- Defective gas exchange $\rightarrow$ $\downarrow$ PaO₂ $\pm$ $\uparrow$ PaCO₂ $\pm$ $\downarrow$ pH.

III- Factors which predispose to the attack:

1- Extrinsic factors:

- Inhalants : e.g. dust, fumes, pollens, mites and smoke
- Ingestants : e.g. food additives
- Injectants : e.g. drugs
- Infection : e.g. viral upper respiratory infection.

2- Intrinsic factors:

- Exercise: Due to dryness of the airways $\rightarrow$ release of chemical mediators.
- Psychogenic: Due to emotional factors.

☆ Clinical picture of asthma:

○ Symptoms:

- Paroxysmal attacks of cough, dyspnea and wheezes may be acute following exposure to allergens or gradual onset after URTI.
The attacks may be induced by exercise, psychic troubles or without any stimulus.
- Inbetween the attacks the child is usually free but may experience some symptoms in chronic "persistent" asthma.

○ Signs:

1- General signs:

- Irritability and restlessness (drowsiness in severe attacks).
- Sign of respiratory distress (according to severity).

2- Chest examination:

- The same as acute bronchiolitis.

N.B. In both asthma and bronchiolitis:

- * The signs are bilateral (opposite to F.B.)
- * Liver and spleen may be felt in abd. exam. due to hyperinflated lung which displace the diaphragm downward but liver span is normal (Opposite to H.F. in which hepatomegaly occurs, so $\rightarrow$ $\uparrow$ liver span).

☆ Classification of asthma severity:

	Symptoms	Nocturnal symptoms	FEV ₁ or PEF
Severe Persistent	Continuous Limited physical activity	Frequent	≤ 60% predicted Variability > 30%
Moderate Persistent	Daily Attacks affect activity	> 1 time week	60 - 80% predicted Variability > 30%
Mild Persistent	> 1 time a week but < 1 time a day	> 2 times a month	≥ 80% predicted Variability 20 - 30%
Intermittent	< 1 time a week Asymptomatic and normal PEF between attacks	≤ 2 times a month	≥ 80% predicted Variability < 20

☆ Classification of asthma exacerbation:

	Mild	Moderate	Severe
Resp. distress	-Mild	- Moderate	- Severe
Dyspnea	-While walking	- While talking	- At rest
Pulse BPM	- <100	-100-120	- >120
Auscultation	-Expiratory wheeze	- Both insp. & exp.	- No audible sounds
Pulmonary function	-± normal	- Moderately ↓↓	- Severely ↓↓
PEFR	-> 80 %	- 60-80%	- < 60%
O ₂ saturation	-> 95%	- 90-95%	- < 90%
Pco ₂	- <45 mmhg	- <45 mmhg	- > 45 mmhg

☆ Investigations: (Mainly clinical diagnosis)

1- Laboratory: Rarely needed

- ↑ eosinophils and IgE in blood and sputum.
- Skin testing to the allergens.
- Radioallergosorbent test (RAST): a radioimmunoassay test to detect specific IgE antibodies to suspected or known allergens.

2- Assessment of severity:

- X-ray chest: Hyperinflation ± areas of collapse (during the attack)
- ABG's:
 - ↓ PaO₂ → in mild to moderate attacks.
 - ↓ PaO₂ ± ↑ PaCO₂ ± ↓ pH → in severe attacks.
- Pulmonary function:
 - Forced expiratory volume (1 sec.) (FEV₁) → ↓.
 - Peak expiratory flow rate (PEFR) → ↓

☆ **Do all children who wheeze before the age of 3 years have asthma?**

- According to the modified *Asthma Predictive Index* (API), a child has a positive index if there is:
 - 1) A history of four or more episodes of wheezing. At least one or more of the episodes needs to be confirmed by a doctor.
 - 2) The presence of at least one major or two minor criteria

Major Criteria:

- a. Having a parent with the diagnosis of asthma.
- b. The child has eczema (diagnosed by a physician)
- c. The child is allergic to one or more pollens, molds, dust mites verified by allergy skin test or blood test)

Minor Criteria:

- a. A history of wheezing without having a cold
 - b. A blood test showing elevated eosinophils (4 or more percent of total white blood cells)
 - c. Allergic sensitivity to milk, egg or peanut (verified by allergy skin test or blood test)
- *A positive API strongly suggests a child will have persistent or recurring wheezing (asthma).*
 - *A negative API means asthma and persistent wheezing beyond age 5 is very unlikely.*

☆ **D.D.:**

- 1- Causes of wheezy chest esp. bronchiolitis.
- 2- Causes of paroxysmal cough e.g. F.B. and pertussis.

☆ **Complications:**

- 1- Lung: collapse, emphysema, 2ry infection and respiratory failure.
- 2- Pleural: pneumothorax.
- 3- Heart: heart failure.

☆ Treatment of bronchial asthma:

A) Drugs used in bronchial asthma

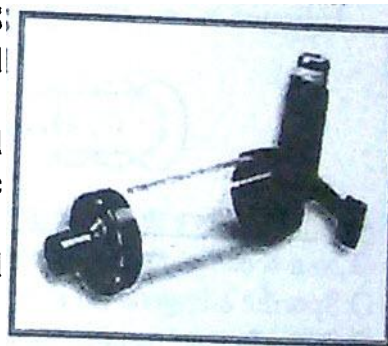
Drugs used in treatment are either relievers that relieve acute attack or controller drugs that are used for long term control.

I- Bronchodilators:

	Mechanism of action	Side effects
- Adrenaline	⇒ (α, β stimulant) ++ adenylyl cyclase	⇒ Hypokalaemia, tachycardia tremors, pallor & palpitation
- Salbutamol and terbutaline	⇒ Short acting selective β_2 stimulants.	⇒ Few side effects of adrenaline
- Salmeterol and formoterol	⇒ Long acting selective β_2 stimulants.	⇒ As salbutamol
- Ipratropium Bromide	⇒ Parasympatholytic	⇒ Mild atropine like action
- Theophylline	⇒ • -- phosphodiesterase • ++ release of Catecholamines	⇒ - Tachycardia - GIT upsets - Convulsions

II- Anti-inflammatory:

- Steroids are strong anti inflammatory drugs that ↓↓ bronchial oedema and inflammatory process. It also facilitate the action of other bronchodilators.
- Either: * Injection → (Hydrocortisone) → (In short term ttt).
- * Inhaled corticosteroids (ICS): e.g beclomethasone and fluticasone.
- Recent guidelines recommend daily ICS therapy as the treatment of choice for all patients with persistent asthma .
- Adverse effects from ICSs are local: oral candidiasis (thrush) and dysphonia (hoarse voice).
- These drugs can be delivered with metered dose inhaler (MDI) with or without spacer.



* Systemic (oral) → prednisone (High effect) & ↑ S.E. in long term use.

III- Mast cell stabilizers:

- Used as a prophylaxis before the attack to prevent mast cell degranulation (prevent but not treat the attack) e.g. Na Cromoglycate "inhalation"

IV- Leukotrien modifiers:

- Used as a prophylaxis before the attack and improve pulmonary function.
- Either: * Zafirlukast. * Montelukast (Singular).

V- Omalizumab : a humanized monoclonal antibody that binds IgE.

B- TTT of acute attack (Quick relievers)

1- Mild asthma:

- β_2 agonist → (nebulizer, oral or aerosol).

2- Moderate - severe asthma:

- β_2 agonist + inhaled parasympatholytics or theophylline (oral, IV or suppositories)
- Short course of systemic steroids (3-4 days).
- If the attack is severe consider hospitalization & oxygen.

3- Status asthmaticus:

"Increasingly severe asthma not responding to initial drugs within 24 hours"

Clinical picture: the same as acute severe asthma with signs of respiratory failure (confusion, bradycardia, paradoxical thoraco-abdominal respiration, cyanosis,...).

- Admission to ICU
- Monitoring of RR, pulse, cyanosis and chest signs.
- Performing X-ray chest, PEFR and ABG's
- O_2 therapy + IV fluids (add K as β_2 agonists lead to hypokalaemia).
- Bronchodilators: Salbutamol nebulizer can be delivered frequently (every 20 min to 1 hr) or continuously. Ipratrobium bromide is added to cause synergistic action.
- Parenteral steroids (IV methyl prednisolone or hydrocortisone) followed by short term oral steroids.
- Parenteral antibiotics in 2ry infection.
- In case of failure to respond to above lines we have 3 options
 - A) Aminophylline continuous infusion 1mg/kg/h
 - B) Adrenaline SC 0.01 ml/kg
 - C) Mg Sulfate IV infusion over one hour.
- Mechanical ventilation (better with pancuronium paralysis):
Indicated in → respiratory failure, cyanosis or marked ↓ of PaO_2 .

C) Measures inbetween the attacks

1- Avoid exposure to triggering agents:

- Non specific: smoke, perfumes, tobacco,
- Specific allergens (in known atopic individuals).
- TTT of upper respiratory infection.
- In exercise induced asthma.
 - Salbutamol inhalation (10 min. before exercise).
 - Or - Na Cromoglycate (15 min before exercise).
 - Or - Monteleukast oral (1 hour before exercise).

2- Stepwise approach for managing asthma:

	Long term control
Step 1 Intermittent	Not usually needed
Step 2 Mild persistent	- Low dose inhaled steroids or Na cromoglycate or Leukotriene modifiers
Step 3 Moderate persistent	- Moderate dose inhaled steroids or - Low dose inhaled steroids + one of the following: * Long acting B ₂ * Leukotriene modifiers
Step 4 Severe persistent	- High dose inhaled steroids + one of the following: * Long acting B ₂ * Sustained release theophylline * Leukotriene modifiers <u>N.B.:</u> If no improvement long term oral steroids may be indicated.

☆ Prognosis:

- Gradual decline of the attacks with age occurs in 2/3 rd of patients.
- Atopic patients and steroid dependent carry a poor prognosis.

Noisy Breathing

	Character	Due to	Causes
* Snoring	• Inspiratory irregular sound	• Partial obstruction of the nose and nasopharynx.	- Adenoid enlargement. - Nasal allergy, polyp or inflammation.
* Stridor	• Inspiratory (± exp.) continuous harsh sound	• Partial obstruction of larynx or trachea.	- Causes of stridor "see before"
* Rattling	• Inspiratory (± exp.) irregular coarse sound	• Partial obstruction of major bronchi by secretions.	- Causes of crepitations on auscultation (e.g. pneum.)
* Wheezing	• Expiratory musical continuous sound	• Partial obstruction at the level of small bronchi and bronchioles	- Causes of wheezes on auscult. (see below)
* Grunting	• Early expiratory short sound.	• Forced expiration against closed epiglottis.	- Causes of severe (grade III) respiratory distress.

Wheezy Chest

☆ Def.:

Continuous expiratory musical sound caused by partial obstruction of the small bronchi and bronchioles.

☆ Grades of wheezing:

- Grade I → Wheezing only "No respiratory distress"
- Grade II → Wheezing with tachypnea
- Grade III → Wheezing with retraction.
- Grade IV → Wheezing with cyanosis.

☆ Causes:

Z Acute wheezing

- 1- The 1st attack of asthma.
- 2- Acute bronchiolitis.
- 3- Foreign body inhalation.
- 4- Acute congestive heart failure.
- 5- Severe bronchopneumonia.

Z Chronic or persistent wheezing

- 1- Bronchial asthma.
- 2- Bronchiolitis obliterans
- 3- Foreign body inhalation.
- 4- Recurrent or chronic heart failure.
- 5- Bronchopulmonary dysplasia.
- 6- Recurrent aspiration:
(Esp. infant with GERD or pharyngeal in-coordination)
- 7- Chronic chest diseases (e.g. cystic fibrosis and T.B.)

☆ How to approach the diagnosis:

I- Is it wheezy chest or not:

The sound must be differentiated from other causes of noisy breathing.

II- History:

- ⊥ Asthma →
 - * +ve family history.
 - * Recurrent cough, dyspnea and wheezes.
 - * Symptoms related to allergens or exercise.
- ⊥ Acute bronchiolitis →
 - * Age of onset below 2 years.
 - * Mostly in winter and spring.
- ⊥ F.B. inhalation →
 - * Common age: 3 months- 6 years.
 - 1- Initially: cough, choking, gagging, wheezes or stridor.
 - 2- F.B. pass to smaller airways (silent phase)
 - 3- Then: recurrent attacks of wheezes, distress, pneumonia.
- ⊥ Heart failure →
 - * History of cardiac lesion.
 - * Manifestations of heart failure (e.g. lethargy, dyspnea, oedema,).
- ⊥ Bronchopneumonia →
 - * History of sudden or acute onset fever, cough and expectoration.
- ⊥ Cystic fibrosis →
 - * +ve family history may present (AR).
 - * Associated GIT manifestations.
- ⊥ T.B. →
 - * Contact of a known case of T.B.
 - * Emaciation and bad general condition.

III- Examination:

- ⊥ Asthma.
 - ⊥ Bronchiolitis.
 - ⊥ Heart failure.
 - ⊥ Bronchopneumonia.
 - ⊥ T.B.
 - ⊥ F.B. inhalation → It may present with any sign according to the site and degree of airway obstruction e.g. unilateral emphysema, collapse or even pneumonia or abscess.
 - ⊥ Cystic fibrosis → Associated findings e.g. nasal polyps, rectal prolapse or may be DM.
- } → Discuss.

IV- Investigations:

- 1- X-ray chest: for all cases (discuss).
- 2- For the cause: ⊥ Bronchoscopy: For F.B.
 - ⊥ ABG's: For severe asthma, bronchiolitis or H.F.
 - ⊥ Culture and sensitivity: For bronchopneumonia.
 - ⊥ Sweat chloride test: (Cl in sweat > 60 meq/L) in cystic fibrosis.
 - ⊥ Investigations for T.B.

☆ Treatment:

- ⊥ TTT of bronchial asthma, bronchiolitis, H.F, bronchopneumonia, T.B. or GERD.
- ⊥ Bronchoscopic extraction of F.B.
- ⊥ Respiratory support + antibiotics for cystic fibrosis.

Diseases of the Pleura

1- Dry Pleurisy

☆ **Aetiology:**

- 1- Infection: viral or bacterial pneumonia, T.B and URTI.
- 2- Collagen diseases: rheumatoid arthritis, SLE and rheumatic fever.
- 3- Inflammatory lesions: (e.g. abdominal or thoracic wall abscess).
- 4- Trauma: to the chest wall.

☆ **Pathology:**

- ⊥ Thick, rough and lusterless pleura.
- ⊥ Some times adhesions between visceral and parietal layers of pleura occur esp. in T.B.
- ⊥ In severe cases fibrosis is extensive → limitation of chest movements.

☆ **C/P:**

- ⊥ Manifestations of the cause.
- ⊥ Stitching pain ↑↑ with cough, sneezing and deep respiration.
- ⊥ Chest examination may reveal ↓ air entry on the affected side and pleural rub is auscultated (superficial, to and fro scratchy sound ↑ by respiration and ↓ by holding breath).

☆ **Treatment:**

- ⊥ Of the cause.
- ⊥ Analgesics for chest pain.

2- Pleural effusion (serofibrenous pleurisy)

☆ **Aetiology and pathology:**

1- **Transudate:**

- Criteria → clear/↓ sp. gravity (< 1015)/↓ ptn. (< 3 gm%)/few cells / no organism
- Causes → Generalized oedema(Cardiac , renal and hepatic).

2- **Exudate:** (Empyema)

- Criteria → turbid/ ↑ sp. gravity (>1015)/ ↑ ptn.(<3 gm%)/ ↑ cells / ± organism
- Causes →
 - 1- Chest infection: pneumonia, T.B.,
 - 2- Ruptured lung abscess, trauma or mediastinitis.
 - 3- SLE
 - 4- Uremia.
 - 5- Malignancy
 - 6- Pulmonary infarction.

3- **Hemothorax:**

- Criteria → Bloody effusion
- Causes → 1- Trauma 2- Tumours 3- T.B. 4- Hgic blood diseases

4- **Chylothorax:**

- Criteria → White milky effusion, dissolves in ether & stained by Sudan III.
- Causes → Rupture thoracic duct due to trauma or tumours.

☆ **C/P:**

- 1 **Symptoms:**
- Of the cause (e.g. fever, cough, dyspnea, ...).
 - Disappearance of stitching chest pain (if 2ry to dry pleurisy) ± appearance of dull aching pain.
 - The patient usually lie on the affected side (trecpopnea).
- 1 **Examination:**
- Signs of RD in massive pleural effusion.
 - See before (Insp./Palp./Perc./Ausc.)
 - N.B. if pneumonia is the underlying cause adventitious sounds may be auscultated.

☆ **D.D.:**

- 1 Other causes of RD esp. pneumonia & collapse.

☆ **Investigations:**

- 1- **For the cause.** e.g Tuberculin test
- 2- **X-ray chest:** Homogenous opacity obliterating the costophrenic angle rising to the axilla. + shift of the mediastinum (trachea and heart) to the opposite side.
- 3- **Chest ultrasound** which is very sensitive in detecting amount of effusion.
- 4- **Thoracocentesis:**
 - To detect the character of fluid (describe).
 - For culture and sensitivity if infected.
- 5- **Pleural biopsy:** Is very helpful in the diagnosis of TB and malignancy.
- 6- **Thoracoscopy & bronchoscopy:** Is of value especially in malignant effusion and possibly in cases of tuberculous etiology.

☆ **Treatment:**

- 1- TTT of the cause.
- 2- Symptomatic treatment for fever, cough and dyspnea.
- 3- Drainage "thoracocentesis"
 - In massive effusion with marked resp. distress.
 - Effusion not resolved by medical treatment.
 - In hemothorax and empyema drainage should be done as rapid and as complete as possible.

N.B.

- ✧ Effusion due to pneumonia may be:
- 1- At the same time of pneumonia → synpneumonic effusion.
 - 2- After resolution of pneumonia → metapneumonic effusion.
- ✧ In T.B. effusion thoracocentesis is not recommended as it may lead to fistula formation.
- ✧ The recommended site of aspiration of effusion is 5th space MAL or scapular line.

3- Empyema "Purulent Pleurisy"

☆ Aetiology and pathology:

Exudative pleural effusion "Describe".

☆ C/P:

⊥ As pleural effusion but →

1- More ill and toxic patient

2- Massive chest wall oedema (+ve Bothina sign).

3- If penetration of the visceral pleura occurs it will lead to formation of bronchopleural fistula and expectoration of huge amount of pus.

☆ Investigations:

1- For the cause:

2- X-ray chest: The same as effusion but:

♦ Opacity may be more dense.

♦ Rib crowding on the affected side.

♦ Mediastinum is shifted to other side but may be to the same side if associated with lung collapse or fibrosis (chronicity or malignancy).

3- Thoracocentesis: The fluid is exudate "see before".

☆ D.D.:

⊥ From other causes of RD

⊥ From pleural effusion.

☆ Treatment:

⊥ Of the cause.

⊥ Antibiotics according to C. & S. of pleural pus.

⊥ Throcoentesis: closed drainage (under water seal) for at least one week, more than one tube may be needed to drain pockets of pus.

⊥ Recently the treatment modality of choice is intrapleural placement of pigtail catheter and administration of tissue plasminogen activator (tPA).

☆ Complications:

1- Pyoneumothorax or bronchopleural fistula "open into the lung"

2- Chronicity "fibrothorax".

3- Spread of infection: mediastinitis,

4- Pneumothorax

☆ **Pathology:** Presence of air in the pleural cavity.

☆ **Aetiology:**

- 1- Trauma to the chest wall.
- 2- Thoracocentesis.
- 3- Rupture pneumatocele in staph pneumonia.
- 4- Rupture lung abscess or T.B. cavity.
- 5- Rupture of surface alveoli esp. in emphysema or vigorous resuscitation of neonate.

☆ **C/P:**

└ **Symptoms:**

- 1- Asymptomatic: Discovered accidentally.
- 2- Symptomatic: * Resp. distress * Symptoms of the cause.

└ **Examination:** See before.

☆ **Investigations:**

└ For the cause

└ X-ray chest → Jet black hypertranslucency with shift of the mediastinum to the opposite side.

☆ **Treatment:**

└ Of the cause.

└ Asymptomatic: No ttt "spontaneous resolution"

└ Symptomatic : Closed drainage "under water seal" → tube inserted in 2nd space.

5- Hydropneumothorax

☆ **Pathology:** "Both fluid and air in the pleural cavity"

☆ **Aetiology:**

└ Thoracocentesis for pleural effusion → hydropneumothorax.

└ Thoracocentesis for hemothorax → hemopneumothorax.

└ Pneumonia or empyema with broncho-pleural fistula → pyopneumothorax.

└ Penetrating chest injury.

☆ **C/P:**

└ **Symptoms:**

- 1- Of the cause
- 2- Respiratory distress.

└ **Examination:**

- 1- Of the cause
- 2- Of hydropneumothorax "see before".

☆ **Investigations:**

- 1- For the cause.
- 2- X-ray chest → Air-fluid level.

☆ **Treatment:**

- 1- Of the cause + antibiotics according to C & S
- 2- Drainage under water seal till fistula healing.
- 3- Surgery is indicated to close the fistula if closed drainage is failed.

Respiratory Failure (RF)

- **Def:** Failure of the lung to maintain normal arterial levels of O₂ and CO₂.

- **Causes:**

Type I "Peripheral RF"

- ♦ Airway obstruction e.g. FB, asthma
- ♦ Parenchymal dis. e.g. pneumonia
- ♦ Restrictive lung dis. e.g. pneumothorax, pleural effusion.

Type II "Central RF"

- ♦ Brain (drugs, hge, infection)
- ♦ Neuromuscular (SMA, GBS)
- ♦ Skeletal (severe kyphosis or scoliosis)

- **C/P:**

- 1- of the cause.
- 2- of hypoxemia (Pallor, agitation,)
- 3- of hypercapnia (Headache, confusion, coma)
- 4- Respiratory pattern (RD in type I & Shallow respiration in type II).

- **Diagnosis:** ABG's (↑ PaCO₂, ↓ PaO₂, ↓ pH).

- **Treatment:** → (ABC / of the cause / O₂ therapy).

Foreign body inhalation

Its sequelae are dependent on their nature, location and degree of obstruction.

<i>Expelled immediately</i>	<i>Larynx</i>	<i>Tracheal</i>	<i>Bronchial</i>
By reflex cough	♦ large: complete obstruction → suffocation ♦ small: partial obstructions: - Hoarseness - Stridor and R.D - Aphonia	Cough R.D and cyanosis	♦ Partial obstruction → Wheezy chest ♦ Complete obstruction → Collapse followed by infection (abscess-pneumonia)

*** Diagnosis:**

- 1) **History:**
- sudden onset with no preceding illness.
 - history of choking and cough.

2) **Physical examination:**

- F.B. inhalation may have any chest presentation e.g stridor, wheezy chest, pneumonia, lung abscess & collapse or unilateral emphysema.
- F.B inhalation should be put in mind in any chest case with:
 - * Chronic or recurrent chest infection
 - * Wheezy chest not responding to treatment
 - * Unexplained lung collapse

3) **Investigations:**

1. Laryngeal obstruction: by laryngoscope
2. Tracheal or bronchial F.B.: by bronchoscope

*** Treatment:**

- Emergency treatment : See emergency chapter
- Removal of FB by laryngoscopy or bronchoscopy
- Proper antibiotics for underlying infection

III- TUBERCULOSIS

☆ Definition:

Chronic infectious disease, which can occur at any age with wide range of clinical presentations.

☆ Aetiology:

① Causative organism:

- ✧ Mycobacterium T.B. bacilli (human and bovine types).
- ✧ Acid fast, alcohol fast, aerobic intracellular bacilli.
- ✧ High content of lipid is present in the bacilli so resist ttt.

② Mode of transmission:

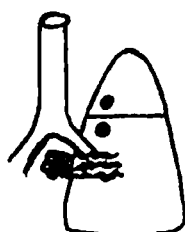
- 1- Inhalation → pulmonary and tonsillar T.B.
- 2- Ingestion (esp. milk) → intestinal T.B.
- 3- Wound contamination → skin T.B.
- 4- Haematological spread → from 1ry T.B. focus.
- 5- Transplacental → very rare (if occur the 1ry lesion will be foetal liver).

③ Predisposing factors:

- 1- **Organism related factors:** ✧ Virulence ✧ Number of the bacilli.
- 2- **Host related factors:**
 - ✧ Age: Below 5yrs and above 15 years.
 - ✧ Sex: male > female.
 - ✧ Race: common in Negroes.
 - ✧ Socioeconomic state: poor living standard and bad housing
 - ✧ Chronic illness: e.g. AIDS and DM, ↑ susceptibility for T.B.
 - ✧ Immunodeficiency: Malnutrition and prolonged steroid ttt.

☆ Pathogenesis:

- 1- The response of exposure of previously uninfected child to TB bacilli is formation of (**1ry complex**) at the site of entry of bacilli:



a- Lung "1ry pulmonary complex"

- * 1ry focus (Ghon's focus) → subpleural in the lower part of the upper lobe or the upper part of the lower lobe.

* Lymphangitis.

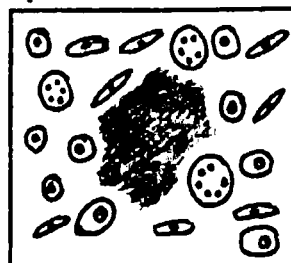
* Regional lymphadenitis "Hilar L.N."

b- Tonsils "1ry cervical complex"

c- Intestine "1ry mesenteric complex"

2- Tubercle is formed of:

- ✧ Central caseation
- ✧ Epithelioid cells.
- ✧ Macrophages and lymphocytes.
- ✧ Langerhans giant cells (aggregation epithelioid cells).



3- Fate of primary complex:

✧ Regression (90%):

- With good immunity → healing of the lesion
 - If small → complete fibrosis.
 - If large → capsulation and calcification which include viable bacilli that may remain dormant for long period.

✧ Progression (10%):

- Direct spread → * T.B. pneumonia and pleural effusion.
- Bronchial spread → * Incomplete obstruction → emphysema.
* Complete obstruction → collapse.
- Hematological spread → * One organ affection.
* Miliary T.B.

4- Differences between children and adults regarding 1ry complex:

- Adult 1ry complex is usually apical, heal by fibrosis with less nodal involvement and rare hematological spread.

☆ Diagnosis of T.B.:

1- History:

- ✧ History of contact with known case of T.B.
- ✧ Low socio-economic class.
- ✧ History of vaccination (may be negative).
- ✧ Non specific manifestations (Night fever & sweating, anorexia, weight loss,...)

2- C/P: According to the site involved (see later).

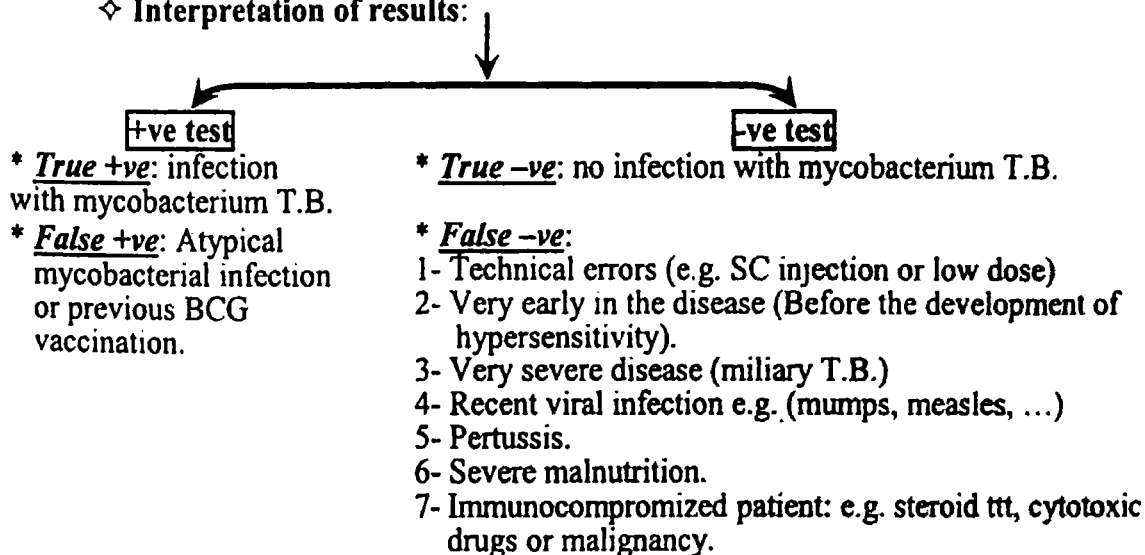
3- Blood: Support the diagnosis

- ✧ ↑ ESR
- ✧ +ve CRP.
- ✧ Lymphocytosis.

4- Tuberculin skin test:

- ✧ Idea: Delayed hypersensitivity reaction to tuberculoprotein.
- ✧ Method: Mantoux test: 0.1 ml purified protein derivative (PPD) containing 5 tuberculin units are injected intradermally in the medial side of the forearm. The result is obtained after 48-72 hours.
- ✧ Results: Indurated area (not erythema)

✧ Interpretation of results:



❑ Definitions of Positive Tuberculin Skin Test (TST)

⊕ Induration ≥ 5 MM

- ↳ Children in close contact with tuberculous patients.
- ↳ Children suspected to have tuberculosis disease(clinical or in CXR).
- ↳ Immunocompromized children.

⊕ Induration ≥ 10 MM

- ↳ Children younger than 4 yr of age
- ↳ Children with other medical conditions, including Hodgkin disease, lymphoma, diabetes mellitus, chronic renal failure, or malnutrition.
- ↳ Children from endemic area or exposed to persons from endemic area.

⊕ Induration ≥ 15 MM

- ↳ Children 4 yr of age or older without any risk factors.

5- X-ray chest:

- ◇ Iry pul. T.B.
 - ⊕ Enlarged hilar LN
 - ⊕ Irregular round shadow at any part of the lung.
- ◇ Miliary T.B. → mottling opacities (snow flakes opacities).
- ◇ T.B. bronchopneumonia → fluffy cotton appearance.
- ◇ Other findings → emphysema, collapse, pleural effusion or bronchiectasis.

6- Specific investigations according to site:

- ◇ Pleural aspirate in T.B effusion (commonly exudate /+ve culture in 50%)
- ◇ Fundus examination in miliary T.B.(choroid tubercles).
- ◇ CSF in T.B. meningitis
 - ⊕ Turbid + web on standing.
 - ⊕ ↑↑ protein + ↑↑ cells (lymphocytes_
 - ⊕ ↓↓ glucose + ↓↓ chloride.

7- Detection of the organism:

- ◇ Isolation from (sputum, gastric aspirate, CSF, pleural fluid or urine). The most commonly used method in children is gastric aspirate in early morning for 3 days.
- ◇ Specimen is examined by:
 - ⊕ Zeil Nelson staining and microscopy.
 - ⊕ Culture on Lowenstein Jensen media.
 - ⊕ Guinea pig inoculation.
 - ⊕ Recently:
 - * Polymerase chain reaction (PCR).
 - * High performance liquid chromatography.
 - * Bactec culture method.
 - * Interferon γ release assay using Quantiferon.
 - * Phage technology (FAST Plaque TB).

☆ Management of T.B.:

I- Prophylaxis:

- ◇ BCG vaccination. ◇ Avoid contact with known cases.
- ◇ Milk sanitation. ◇ Improving public health (Adequate nutrition, exercise,...)
- ◇ INH chemoprophylaxis: 10-15 mg/kg/day for 6 months given for contacts to known T.B. case.

II- General lines of treatment:

- ◇ Bed rest in active disease.
- ◇ Adequate nutrition with vitamin and mineral supply.
- ◇ Healthy environment with exposure to sun and fresh air.

III- Specific treatment:**A- Antituberculous drugs****1st line drugs**

- 1- Isoniazide (INH): 10-20 mg/k/oral
* S.E. (hepatotoxicity and peripheral neuritis responds to pyridoxine)
- 2- Rifampicin: (10-20 mg/k/oral)
* S.E. (Hepatotoxicity and red staining of body fluids).
- 3- Pyrazinamide (20-40 mg/k/oral)
* S.E. (Hepatotoxicity, hyperuricaemia)

Alternative drugs

- 1- Streptomycin (20-40 mg/k I.M.)
S.E. (ototoxic, nephrotoxic)
- 2- Ethambutol (15-20 mg/k/oral)
S.E. (optic neuritis so not given < 5 yrs)
- 3- Ethionamide (15-20 mg/k/oral)
S.E. (GIT and hepatotoxicity)
- 4- Cycloserine (5 mg/k/oral)
S.E. (Psychosis and convulsions)
- 5- Para amino salicylic acid (PAS) not recommended due to severe GIT manifestations (ulceration, bleeding,)

B- Regimens of therapy

- 1- Single drug therapy: INH for 6 months (in TB infection without disease e.g. positive tuberculin test only without clinical or radiological manifestations).
- 2- Double drugs therapy: INH + Rifampicin (9-12 months) → not recommended.
- 3- Triple drug therapy: INH + Rifampicin + pyrazinamide for 2 months (for 6-9 months).
- 4- Quadriple drug therapy: Add streptomycin for 2 months to the previous regimens (esp. in resistant strains).

C- Corticosteroids

- * Prednisone 2 mg/k/day for 4-6 weeks then gradual withdrawal + other antituberculous drugs
- * Indicated in:
 - * Miliary T.B.
 - * Enlarged hilar LN with airway obstruction.
 - * T.B of serous membranes (T.B. pleurisy, pericarditis or meningitis).
 - * T.B. adrenal (to prevent Addisonian crises).

IV- Follow up:

- ✧ Clinical and radiological response to ttt not appear before 2-3 weeks.
- ✧ ESR, CRP and clinical response are valuable for follow up.

☆ Clinical presentations of T.B.:**1- Pulmonary T.B.**

- ✧ Asymptomatic
- ✧ Manifestations of toxæmia (loss of weight, fever, sweating).
- ✧ Manifestations of hilar LN ++ (emphysema, collapse, +ve Dyspen sign) or rarely cough, expectoration and respiratory distress.
- ✧ Manifestations of extension:
 - * T.B. bronchopneumonia "see before".
 - * T.B. effusion "see before".
 - * Miliary T.B.

2- Intestinal T.B.

Due to ingestion of T.B. bacilli in food (e.g. milk) or swallowed sputum from tuberculous lesion in the lung.

A- Tabes mesenterica:

- ✧ Enlarged mesenteric LN in Rt. iliac fossa → adhere to intestinal loops → heal by fibrosis with 2ry T.B. peritonitis or intestinal obstruction.
- ✧ Clinically: Abd. pain or diarrhea alternating with constipation.
- ✧ Examination: reveals multiple firm ($\pm$ tender) glands in the abdomen.

B- Tuberculous enteritis

- ✧ T.B. ulcers in terminal ileum or cecum.
- ✧ Clinically: chronic diarrhea with offensive stool $\pm$ bloody.
- ✧ Examination: reveals tender abdomen and emaciation.

3- T.B. peritonitis:

- ✧ Due to:
 - * Spread of infection from T.B. enteritis or abd. LN
 - * Spread from T.B. salpingitis.
 - * Blood born (uncommon).
- ✧ 2 types:
 - a- Wet type (ascitic type) →
 ↑ ascitic fluid and ↓ adhesions.
 - b- Dry type (adhesive type) →
 ↓ ascitic fluid and ↑ adhesions.
- ✧ Clinically: Swollen abdomen with ascitis, sausage shaped peritoneal mass may be palpated.

4- T.B. meningitis:

- ✧ Due to: Hematogenous spread either isolated or with milinary T.B.
- ✧ Clinically: Insidious onset commonly in infancy and early childhood.
 Present into 3 stages (each lasts from 1-2 weeks):
 - 1- Prodroma: Non specific manifestations (vomiting, irritability, fever, anorexia,)
 - 2- Stage of meningitis:
 - * Signs of meningeal irritation.
 - * Signs of increase ICT.
 - * Cranial nerve palsies.
 - 3- Terminal stage: Paralysis → coma → $\pm$ death.

5- Miliary T.B.:

- ✧ Due to: Hematogenous spread of T.B. bacilli from 1ry focus (usually pulmonary), presented within one year of primary infection if not treated.
- ✧ Clinically:
 - * Very bad general condition with very high fever.
 - * Multiorgan involvement (Respiratory, meningitis, abdominal,...)
 - * Hepatosplenomegaly and lymphadenopathy may present.

6- Other forms of T.B.:

- ✧ Genito-urinary.
- ✧ Pott's disease of the spine.
- ✧ T.B. lymphadenitis.

CHAPTER (VII)

NEUROLOGY

I- SEIZURES (Convulsions)

☆ **Def:**

Paroxysmal involuntary disturbance of brain function, manifested by abnormal motor activities, sensory disturbance, autonomic dysfunction or behavioral abnormalities.

☆ **Aetiology:****A- Acute convulsions**1- **Febrile convulsions**2- **First epileptic fit.**3- **CNS causes:**

- ⊕ Infection: Meningitis, encephalitis and brain abscess
- ⊕ Irritation: Brain oedema.
- ⊕ Tumours of the brain.
- ⊕ Toxic: e.g. tetanus or drugs (aminophylline and antihistamines).
- ⊕ Hge: Trauma, rupture aneurysm and Hgic blood diseases.
- ⊕ Hypoxia: Asphyxia, apnea,
- ⊕ Hypertensive encephalopathy, uraemic encephalopathy,

4- **Metabolic:**

- ⊕ Hypo (glycaemia, calcaemia, magnesaemia).
- ⊕ Hypo or hypernatraemia.
- ⊕ Pyridoxine (B6) deficiency.

B- Recurrent convulsions1- **Recurrent febrile convulsions.**2- **Epilepsy & conditions mimic epilepsy.**3- **Tetany.**4- **Chronic metabolic causes:**

- ⊕ Recurrent hypoglycaemia (Hyperinsulinism, hypopituitarism, glycogen storage diseases).
- ⊕ Uraemic encephalopathy (CRF).
- ⊕ Hepatic encephalopathy.
- ⊕ Inborn errors of metabolism (Phenyl ketonuria, hyper-ammonaemia, maple syrup urine disease,

FEBRILE CONVULSIONS

☆ Def:

Convulsions in children due to rapid increase of body temperature due to extracranial cause (e.g. tonsillitis, pneumonia, ...)

☆ Incidence:

- ⊕ 4% of children.
- ⊕ Family history in about 20% of cases.

☆ Diagnosis:

1- Age: 6 months → 5 years (convulsions below 6 months or above 5 years are not considered febrile).

2- Temperature: usually $> 39^{\circ}$ convulsions occur within 8-12 hours from the onset of fever.

3- No evidence of CNS infection: e.g. meningitis, abscess,

4- Evidence of extracranial infection: e.g. sepsis, tonsillitis,

5- Types of convulsions:

A- Simple febrile convulsions:

- The most common form.
- Usually generalized tonic – clonic.
- Short duration (<15 min.).
- Usually one fit only within 24 hours.

B- Complex febrile convulsions:

- Uncommon.
- May be focal.
- Prolonged duration.
- Fits may recur within 24 hours.

6- Investigations:

Not needed, but complex form may be mistaken with CNS infection, so CSF is done in doubtful diagnosis.

7- D.D.:

Other causes of convulsions.

☆ Treatment:

1- Control of convulsions: Diazepam 0.3-0.5 mg/Kg (I.V. or rectally) .Recently buccal midazolam may be used.

2- Measures to lower body temperature:

☆ Cold backs or baths. ☆ Antipyretic drugs.

3- Treatment of the underlying cause e.g. antibiotics.

4- Prophylactic anti-convulsant therapy e.g. Na valproate.

Not indicated except in complex form. Recurrent cases can be prevented by oral diazepam for 2 days starting from the onset of fever.

☆ Prognosis:

⊕ Recurrence rate about 25%.

⊕ The risk for developing epilepsy is increased with:

- ♦ Family history of epilepsy.
- ♦ Pre-existing neurological disease.
- ♦ Complex form.

EPILEPSY

☆ Def.:

Two or more unprovoked seizures (not related to fever or acute brain insult) greater than 24 hs apart.

☆ Aetiology:

1- Idiopathic (1ry): 80% of cases either hereditary or not.

2- Organic (2ry): 20% of cases, may be:

- ♦ Congenital cerebral malformation.
- ♦ Degenerative brain diseases.
- ♦ Post-traumatic.
- ♦ Post-hgic.
- ♦ Post-infection.
- ♦ Post-toxic.
- ♦ Post-anoxic.

☆ Classification:

1- Focal (partial) seizures:

- * Only one part of the body is involved (focal).
- * Only one type of movements (tonic or clonic).
- * It has 3 types:

a- Simple partial seizures (SPS):	b- Complex partial seizures (CPS):
♦ No aura	♦ Preceded by aura in 1/3 rd of cases (fear, photophobia...).
♦ No automatism.	♦ Automatism may occur (automatic behaviors e.g. chewing, swelling, suckling or aggressive maneuvers).
♦ No loss of consciousness.	♦ Consciousness is impaired.
♦ May be motor, sensory or autonomic fits.	♦ Only motor fits occur.

c- Partial seizures with 2ry generalization:

- ♦ Focal seizures followed by generalization (involvement of whole body).

2- Generalized seizures:

- * Affect the whole body from the start.
- * Classified into:

a- Absence seizures (petit mal):

- ♦ Sudden cessation of all motor activities and speech (Awareness of the surroundings is cut off).
- ♦ Precipitated by hyperventilation or photic stimulation.
- ♦ Rarely persists more than 30 seconds (but frequently recurrent).
- ♦ Usually not associated with loss of consciousness.
- ♦ No aura.
- ♦ No post-ictal phase.

b- Generalized tonic-clonic seizures (Grand-mal): The commonest type, passes into 3 phases:

1- **Aura (pre ictal):** Before the attack as a warning sign which may be motor (localized muscular spasms), sensory (parasthesia) or autonomic (intestinal pain).

2- **Attack (Ictal):**

♦ Sudden loss of consciousness (not more than 10 min).

♦ Tonic phase: Rigid posture with rolling of the eyes, drooling of saliva, clenching of the teeth and incontinence to urine and stool.

♦ Clonic phase: Rapid relaxation and contraction of muscles (clonic motor activity).

3- **Post ictal phase:** Headache, sleep or Todd's paralysis.

c- Myoclonic epilepsy:

Sudden shock like repetitive contractions of group of muscles.

d- Infantile spasms:

Repetitive tonic contractions of the neck and trunk muscles which occur in the first year of life and carry a poor prognosis

e- Atonic seizures:

Sudden loss of body tone and falling down.

☆ Investigations:

1- **Electro-encephalo-gram (EEG)**: must be done for all cases (despite it is -ve in 40%).

It may show specific pattern like

a- 3-spike slow wave complex/sec in absence epilepsy

b- Hypsarrhythmia in infantile spasms.

2- **CT scan or MRI brain**: indicated in: focal lesions (e.g. hge), resistant to ttt evidence of ↑ ICT.

3- **CSF**: Only indicated in suspected CNS infection.

4- **Metabolic screen**: Na, K, Ca, Mg, (to exclude metabolic causes).

5- Recently **functional MRI** to detect the site of epileptic focus.

☆ D.D:

1- **Of causes of recurrent convulsions** esp. conditions mimic epilepsy which are:

- Syncopal attacks.
- Breath-holding attacks.
- Rage attacks.
- Paroxysmal vertigo.
- Pseudo-seizures.

2- **D.D. of the cause** (Idiopathic or 2ry)

☆ Treatment:

I- INBETWEEN THE ATTACKS:

1- **Moderation** of activities and avoidance of the predisposing factors.

2- **Health education** of the parents about the disease and advise them to watch their child during swimming, running, passing the traffic,

3- Drug therapy:

- Only one drug is used in low dose then slightly ↑ if no response.
- If still no response 2nd drug may be tried either alone or in combination with the first drug.
- Duration of therapy is at least for 2 years after the last attack.

Drug	Indications	Dose	Side effects
Na valproate (Depakine)	Broad spectrum	20-40 mg/k/d	General + Hepatotoxicity, alopecia and obesity.
Carbamazepine (Tegretol)	Grand mal and partial	10-20 mg/k/d	General + Hepatotoxicity and eye (diplopia and nystagmus).
Phenobarbitone (Somnialetta)	Broad spectrum	3-8 mg/k/d	General + Rickets, behavioural changes
Phenytoin (Epanutin)	Grand mal	3-8 mg/k/d	General + Rickets, hirsutism & gum hyperplasia
Ethoximide (Zarontine)	Petit mal only	20-40 mg/k/d	General + blood dyscrasias
Clonazepam (Rivotril)	Broad spectrum	0.1 mg/k/d	Increases salivation trachea-bronchial secretions

N.B. ⇒ General side effects of anti-epileptics are:

- Drowsiness
- Ataxia
- GIT disturbances (except Phenobarbitone)

Recent drugs:

Lamotrigine: Used as adjuvant in most types

Vagabatrine: Mainly in infantile spasms

Topiramate: In generalized and partial types

Levetiracetam: Effective add-on therapy.

II- DURING THE ATTACK:

1- **General.** O₂ and suction of secretions.

- 2- **Drugs:**
- Diazepam 0.3-0.5 mg/kg/I.V.
 - If no response → Phenobarbitone 10-15 mg/kg/I.V.
 - If no response → Phenytoin 10-15 mg/kg/I.V.

III- STATUS EPILEPTICUS

Convulsions lasting more than 30 minutes or repetitive convulsions without return of consciousness.

1- **Admission to ICU.**

2- **ABC**

Airway (keep patent airway with suction of secretions).

Breathing (O₂ ± bag and mask ventilation ± pulse oxymetry for O₂ saturation).

Circulation (IV access, IV fluids & blood samples for electrolytes).

3- **Drugs** →

Diazepam (if no response) → phenobarbitone (if no response) → phenytoin (if no response) → Diazepam continuous infusion (if no response) → paraldehyde I.V. (if no response) → General anaesthesia.

II- HYDROCEPHALUS

☆ Definition:

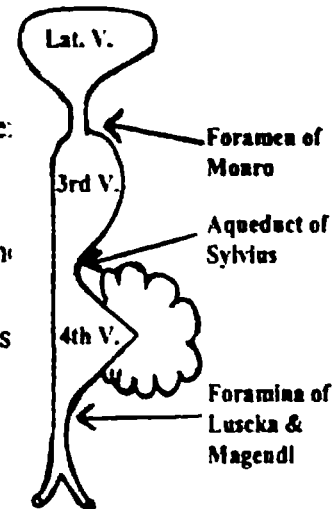
Increase the amount of CSF in the cranial cavity, with or without increase in its tension.

☆ Circulation of CSF:

1- CSF is formed by active secretion by the choroid plexus in the lateral ventricles.

2- **Passage of CSF:** Lat. V. → foramen of Monro → 3rd V. → Aqueduct of Sylvius → 4th V. → Foramina of Luschka and Magendi → Subarachnoid space.

3- CSF is absorbed from arachnoid villi → dural sinuses venous circulation → Heart.



☆ Types and causes of hydrocephalus:

I- Relative hydrocephalus:

Try to brain atrophy, so ↑ the amount of CSF relative to the small sized brain. It is not associated with ↑ in CSF tension (normotensive hydrocephalus).

II- Absolute hydrocephalus:

↑ the amount and tension of CSF (hypertensive hydrocephalus), it will be classified into obstructive or non-obstructive hydrocephalus.

OBSTRUCTIVE (NON-COMMUNICATING)

- | | |
|--------------------------------------|---|
| 1- Foramina of Monro: → | <ul style="list-style-type: none"> • Congenital atresia. • Brain tumours (3rd ventricle T.). |
| 2- Aqueduct of Sylvius → | <ul style="list-style-type: none"> • Congenital atresia. "Common" • Brain tumours (4th ventricle T.). |
| 3- Foramina of Luschka and Magendi → | <ul style="list-style-type: none"> • Congenital atresia (<u>Dandy-Walker malformation</u>). • Congenital downward displacement of cerebellum, medulla and pons (<u>Arnold-Chiari malformation</u>). • Brain tumours (posterior fossa. T.). • Post meningitic adhesions. |

NON OBSTRUCTIVE (COMMUNICATING)

- | | |
|--------------------------------|---|
| 1- Excessive CSF production: → | <ul style="list-style-type: none"> • Tumours of choroid plexus (Papilloma). • Congestion of choroid plexus (Meningitis). |
| 2- Decrease CSF absorption → | <ul style="list-style-type: none"> • Adhesions in subarachnoid space (e.g. post hgc-post meningitic). • Infiltrations in subarachnoid space (e.g. Leukaemia) • Dural sinus thrombosis. |

☆ C/P:A- IN INFANCY AND EARLY CHILDHOOD:

- 1- **Head signs:** Marked (as the sutures are still opened).
 - Large head with progressive increase in size.
 - Wide fontanelles + delayed closure of ant. fontanelle.
 - Widely separated sutures.
 - Scalp veins dilatation.
 - Sun set eyes (forward and downward displacement).
 - Cracked pot sound on skull percussion (Macwen sign).
 - Craniotabes (in all skull bones).
- 2- **Neurological signs:** Mild (as skull enlargement protects against development of marked ↑↑ ICT).

B- IN OLDER CHILDREN

- 1- **Head signs:** Mild as the sutures are not easily separated.
- 2- **Neurological signs:** Manifestations of ↑ ICT:
 - Severe headache esp. in the morning relieved by vomiting.
 - Projectile vomiting, not related to meal, not preceded by nausea.
 - Blurring of vision and papilloedema.
 - Cushing response (Bradycardia & Hypertension).

☆ Diagnosis of hydrocephalus:I- Is it hydrocephalus or not?

Hydrocephalus must be differentiated from other causes of large head (Macrocephaly) which are.

1- Skull causes

- Familial
- Achondroplasia.
- Rickets
- Mucopolysaccharidosis
- Cretinism.
- Ch. hemolytic anemia.

2- Intracranial causes

- ◆ Hydrocephalus
- ◆ Hydranencephaly
(↑ fluid + brain atrophy)
- ◆ Subdural hematoma or effusion
- ◆ Space occupying lesions
(Brain tumours, cyst or abscess).

- * Hydrocephalus can be differentiated from other causes of macrocephaly by:
- a- Clinical examination: (see before) esp. progressive enlargement of the head by serial measurements of head circumference.
 - b- Plain X-ray skull:
 - Before closure of sutures → wide fontanelles and widely separated sutures.
 - After closure of sutures → picture of ↑ ICT (silver-beaten, wide sella turcica).
 - c- Transillumination: +ve in hydranencephaly (may be +ve in marked vent. dilat.)
 - d- Cranial ultrasound: If the fontanelle is still opened.
 - e- C.T. or MRI: Showing hydrocephalus + Identify the cause.

II- Is it obstructive or communicating?**a- Simultaneous lumbar and ventricular manometry:**

If obstructive ventricular pressure will be higher than spinal pressure.

b- Lumbar pneumoencephalography:

Injecting air through lumbar puncture will appear in X-ray skull in communicating (not in obstructive) hydrocephalus.

c - CT or MRI:

The most accurate non invasive method.

☆ Management of hydrocephalus:**I- Medical treatment (Limited value)**

Dehydrating measures (mainly used in communicating):

- ✧ Restriction of salt intake.
- ✧ Carbonic anhydrase inhibitors e.g. Diamox.

II- Surgical treatment

1- Choroid plexectomy: In cases of excess of secretion.

2- Bypass (shunt) operations:

✧ *Types*:

- ♦ Ventriculo-peritoneal shunt.
- ♦ Ventriculo-pleural shunt.
- ♦ Ventriculo-atrial shunt (to Rt. atrium).

✧ *Complications*:

- ♦ Re-obstruction.
- ♦ Infection(staph epidermidis) and sepsis.
- ♦ Nephritis.
- ♦ Shortening of the tube (↑ body size by age).

✧ *Contra-indications for surgery*:

- ♦ Associated lethal extracranial anomalies.
- ♦ Blindness.
- ♦ Cortical thickness less than 1cm.
- ♦ Severe motor or mental Disability.

III- MICROCEPHALY☆ **Definition:**

- ✧ Small head in which head circumference is below the 3rd centile for age and sex.

☆ **Causes:**1- **Primary (Genetic):**

- ✧ Familial (usually AR, may be AD or sporadic).
- ✧ Chromosomal:
 - ♦ Trisomies e.g. 21, 18, 13.
 - ♦ Deletions e.g. Cri-du chat (5 p del.).

2- **Secondary (non-Genetic):**

- ✧ Intrauterine infection: (TORSCH)
- ✧ Intrauterine irradiation: (esp. 1st and 2nd trimester).
- ✧ Intrauterine hypoxia: (Hypoxic-ischaemic encephalopathy).
- ✧ Intrauterine drug exposure: (e.g. hydantoin or alcohol).
- ✧ Meningitis / encephalitis.
- ✧ Metabolic: (Maternal DM, Maternal phenylketonuria).

☆ **Diagnosis:**

- ✧ **History:** ♦ of drugs, irradiation, ♦ Family history.

✧ **Examination**✧ **Investigations for the cause.**

- ♦ TORCH screen
- ♦ MRI brain.
- ♦ Chromosomal study.
- ♦ Metabolic screen.

IV- CRANIO SYNOSTOSIS

☆ Def.:

Early fusion of one or more of skull sutures. If multiple sutures are involved small sized head may result.

N.B. → small sized head may be due to:

- True microcephaly → small brain size.
- Craniosynostosis → early fusion of skull sutures.

☆ Aetiology:

1- Congenital: Isolated or associated with other syndromes e.g. Carpenter syndrome, Crouzon syndrome,

2- Acquired: (uncommon) e.g. Hypercalcaemia.

☆ C/P:

1- Abnormal shape of the skull: (according to the closed suture) may be:

- ✦ Elongated head → Scaphocephaly.
- ✦ Short head → Brachycephaly.
- ✦ Conical shaped head → Acrocephaly.
- ✦ Triangular head → Trigonocephaly.

2- Skull examination:

- ✦ Palpable ridge corresponding to the affected suture.
- ✦ Manifestations of ↑ ICT if multiple sutures are involved.
- ✦ May be small sized head.

☆ Investigations:

1- Skull X-ray:

- ✦ Fusion of sutures.
- ✦ May be ↑ ICT (Silver beaten appearance and wide sella turcica).

2- CT brain:

- ✦ May show hydrocephalic changes (relative).

☆ Treatment:

Surgical separation of skull sutures are indicated in:

- ✦ Cases with hydrocephalus.
- ✦ Cases with progressively ↑ ICT.
- ✦ Cosmotic reasons.

V- MENTAL RETARDATION

☆ **Def.:**

Handicapping disorder with age of onset below 18 years chch by subnormal I.Q. (< 70).

N.B. → I.Q. (Intelligence Quotient) : $\frac{\text{Mental age}}{\text{Chronological age}} \times 100$

☆ **Causes:**

I- **Subcultural:** Children living in low-socioeconomic standard, with poverty & neglect.

II- **Genetic causes:**

- ✦ Brain anomalies: e.g. cong. hydrocephalus, familial microcephaly,
- ✦ Chromosomal anomalies: e.g. Trisomies, deletions,
- ✦ Degenerative brain diseases: e.g. Demyelinating diseases.
- ✦ Errors of metabolism: e.g. aminoacidopathies, lipidosis,

III- **Non-genetic causes:**

➤ **Pre natal:**

- ✦ Congenital infections (TORSCH).
- ✦ Congenital brain malformations.
- ✦ Fetal irradiation or drugs.

➤ **Natal:**

- ✦ Birth asphyxia.
- ✦ Birth trauma "ICH".
- ✦ Hypoglycaemia.

➤ **Post natal:**

- ✦ CNS infection (post-meningitis, post-encephalitis).
- ✦ Kernicterus.
- ✦ Cerebro-vascular accidents.
- ✦ Severe hypoglycaemia or hypernatraemia.

☆ **Manifestations:**

- ✦ Delayed **Social** development → In infancy.
- ✦ Delayed **Speech** → In early childhood.
- ✦ **School** underachievement → In late childhood.

☆ **Investigations:**

For the cause e.g. chromosomal analysis, CT brain, metabolic screen, ...; However with extensive investigations a specific cause is found only in 25% of cases

☆ **Management:**

I- **Prevention:**

- ✦ Proper prenatal- natal and post natal care.
- ✦ Vaccination against rubella for females (not during pregnancy).
- ✦ Neonatal screening to identify preventable causes of MR (e.g. phenylketonuria).
- ✦ TTT of neonatal jaundice, hypoglycaemia,

II- **Treatment:**

No specific ttt, but rehabilitation of the child is depending on degree of MR.

- ✦ Mild MR (IQ 50-70) → Educable (may need special classes)
- ✦ Moderate MR (IQ 35-50) → Trainable (they are trained to care for themselves)
- ✦ Severe MR (IQ 20-35) → ± Trainable.
- ✦ Profound MR (IQ 0-20) → Non trainable (so, they need full time nursing care).

VI- CEREBRAL PALSY "Little Disease"

☆ Def.:

Non progressive disorder of motion and/or posture 2ry to an insult in the developing brain frequently associated with epilepsy, visual and speech defects and mental retardation.

☆ Aetiology.

I- 1ry (Idiopathic) → most cases.

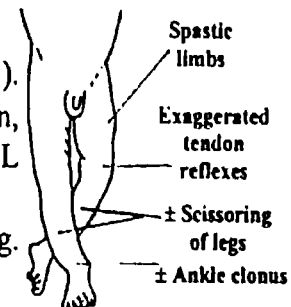
II- 2ry: → the same causes as non-genetic causes of MR (pre natal, natal & postnatal)

☆ Clinical Presentations:

I- Spastic CP (Commonest).

✧ Chch:

- Hypertonia (spasticity) & hyper-reflexia
- Persistence of neonatal reflexes (e.g. Moro & grasp, . .).
- Pyramidal tract manifestations (+ve Babinski sign, exaggerated deep tendon reflexes, clonus & LL scissoring).
- Pseudobulbar palsy (if bilateral) → difficult swallowing.
- It may be:
 - 1- Spastic monoplegia (one limb)
 - 2- Spastic hemiplegia (one side with UL > LL)
 - 3- Spastic paraplegia (both LL).
 - 4- Spastic diplegia (both LL > both UL).
 - 5- Spastic quadriplegia (four limbs).



✧ D.D.:

- Neglected hydrocephalus.
- CNS tumours.
- Spinal cord lesions.

II- Extra-pyramidal CP:

- ✧ Chch →
 - Hypotonia and hyporeflexia
 - Deafness.
 - Choreo-athetotic movements.
- ✧ D.D. →
 - Causes of chorea or athetosis.

III- Ataxic CP:

- ✧ Chch →
 - Hypotonia and hyporeflexia.
 - Ataxia (incoordination of movements, nystagmus, staccato speech and intention tremors).
- ✧ D.D. →
 - Cerebellar ataxia e.g. ataxia telangiectasia & Friedreich ataxia

IV- Atonic CP:✧ **Chch:**

- Severe hypotonia (floppy infant).
- Preserved deep tendon reflexes.

✧ **D.D.:**

- Causes of floppy infant e.g. trisomies, Lowe syndrome, congenital myopathies and spinal muscle atrophy.

V- Mixed type CP: Combination of more than one type.☆ **Diagnosis:**

- ✧ Purely motor disability present since birth or shortly after birth may be associated with epilepsy, MR, deafness or speech defects.
- ✧ Investigations are done mainly to exclude progressive causes of motor disability (e.g. brain tumours, degenerative brain diseases), they include:
 - CT brain or MRI.
 - Fundus exam.
 - Metabolic screen.

☆ **Management:**

1- **Prophylactic** by proper antenatal care.

2- **Management:**

- Physiotherapy.
- Treatment of convulsions if present.
- Muscle relaxant in spastic type e.g. baclofen and Botulinum toxin type A injection recently.
- Rehabilitation according to the degree of MR (mild, moderate, severe or profound) and the degree of motor disability:
 - Class I : No limitation of activity.
 - Class II : Slight to moderate limitation.
 - Class III : Moderate to great limitation.
 - Class IV : No useful physical activity.

VII- ACUTE PARALYSIS**I- Acute asymmetrical paralysis:**

- 1- Poliomyelitis.
- 2- Acute hemiplegia (Stroke).
- 3- Pseudo paralysis (trauma, osteomyelitis,)

II- Acute symmetrical paralysis:**1- Extensive spinal cord compression**

- Trauma to the back.
- Pressure (abscess, tumours,)

2- Familial periodic paralysis**3- Guillain-Barre syndrome:**

- Children above 3 years with preceding upper respiratory viral infection (So called post-infectious polyneuritis).
- Paralysis of ascending nature (L L. → trunk → UL → respiratory).
- Motor > sensory.
- Self limited in a lot of cases (recovery in descending manner).
- C.S.F shows cytoalbuminous dissociation .
- Nerve conduction velocity is markedly impaired.
- TTT: • I.V gamma globulins and plasmapheresis are alternative first lines.
 - Respiratory support till spontaneous recovery occurs.
 - Care of bulbar manifestations.

4- Causes of severe Hypotonia: e.g. Ataxia, chorea.**5- Infections (Diphtheria, Tetanus, Botulism).**

VIII- INABILITY TO WALK

- Walking needs integration between → • CNS
• Muscles
• Skeleton. } ± Training.

I- Central causes

1- Brain

CP, MR, Hydrocephalus, cong. malformations and brain damage (tumours, infections, ...)

2- Spinal cord

- ✦ Congenital → spina bifida.
- ✦ Traumatic → spinal cord trauma
- ✦ Inflammatory → Pott's disease of the spine
- ✦ Neoplastic → spinal cord tumours.

3- Anterior horn cells:

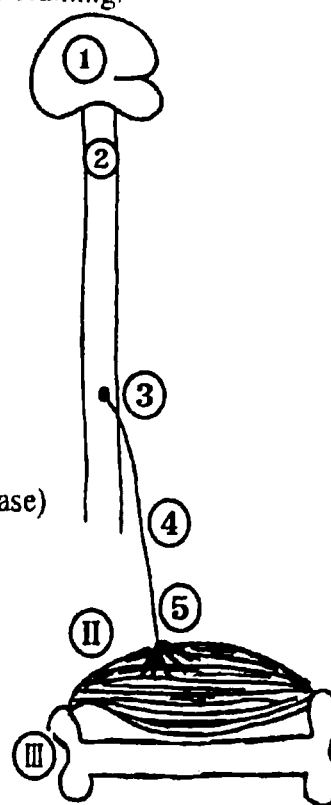
- ✦ Poliomyelitis.
- ✦ Spinal muscle atrophy. (Werdnig – Hoffman disease)

4- Peripheral Nerve:

- ✦ Guillian – Barre syndrome..
- ✦ Polyneuritis (Diphtheria, Drugs, ...)

5- Neuro muscular junction:

- ✦ Myasthenia gravis.
- Botulism
- ✦ Organophosphorus poisoning



II- Muscular causes.

- ✦ 1ry muscle disorders. Myopathies, Metabolic and Myositis.
- ✦ 2ry muscle disorders: Rickets and malnutrition.

III- Skeletal: (Bones, Joints)

- ✦ Trauma (to L.L.)
- ✦ Rickets
- ✦ Inflammation (arthritis, osteomyelitis)

○ D.D. of inability to walk

1ry (The child has not walked before)

I- Paralytic causes

- 1- Early poliomyelitis.
- 2- Early paralysis before walking.
- 3- Cerebral palsy.

II- Non-paralytic causes

- 1- Rickets
- 2- MR
- 3- Simple delayed walking.

2ry (The child has walked before)

I- Paralytic causes

- 1- Poliomyelitis.
- 2- Post (diphtheric, encephalitic or meningitic) paralysis.
- 3- Cerebro-vascular accidents.

II- Non-paralytic causes

- 1- Rickets
- 2- Malnutrition
- 3- Fractures or osteomyelitis

IX- MENINGITIS

- ✧ Inflammation of the membranes covering the brain and the spinal cord.
- ✧ It is classified into:
 - Bacterial meningitis (Due to bacterial infection).
 - Aseptic meningitis (Due to viral or others).
 - T.B. meningitis (Due to T.B.) → see chest.

BACTERIAL (SEPTIC) MENINGITIS

☆ **Def.:**

Acute inflammation of the meninges due to Gram -ve or Gram +ve bacteria chch by purulent exudate.

☆ **Aetiology:**

I- **Gram -ve bacteria:**

- ✧ Cocci → • Neisseria meningitidis (meningococci) → types A, B, C, D, Y & W 135
- ✧ Bacilli → • H. influenza. • E.Coli.

II- **Gram +ve bacteria:**

- ✧ Cocci → • Pneumococci.
- Streptococci (Group A and Group B).
- Staphylococci.
- ✧ Bacilli → • Listeria monocytogenous.

☆ **Epidemiology:**

☞ **Age:**

- ✧ E.coli, Listeria and group B streptococci are the most common forms in the neonatal period.
- ✧ Meningococci and pneumococci are the most common forms in infancy (after 3 months) and childhood.
- ✧ H.influenza is a common cause of meningitis below five years (peak 6-12 months) but the incidence has been declined nowadays due to routine immunization against H.influenza in several countries.

☞ **Incubation period:** usually short (< 7 days), may be longer in H.influnza & Listeria.

☞ **Transmission:**

- ✧ Mostly droplet infection.
- ✧ Rarely blood born (esp. in neonatal meningitis as a sequalae to septicaemia).

☞ **Sporadic pattern of occurrence:** is common for all types except meningococci which occurs in epidemics.

☆ Clinical manifestations:

1- Onset: Abrupt with high fever (may be low grade or even subnormal temp. in young infants)

2- Features of ↑ ICT: see P. 278 (Headache, vomiting, ...)

3- Signs of meningeal irritation:

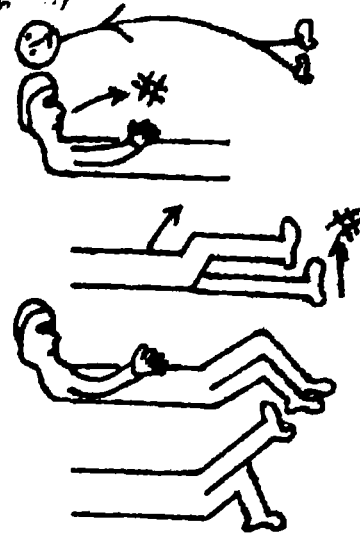
✧ Back stiffness "Opisthotonus"

✧ Neck stiffness "Limited neck flexion"

✧ Kernig's sign "Flexion of the hip prevents knee extension"

✧ Brudzinski neck sign "Passive neck flexion leads to hip and knee flexion"

✧ Brudzinski leg sign "Passive flexion of one hip leads to flexion of other hip and knee"



4- Convulsions: usually generalized, may be the first evidence of meningitis in infants and children

5- Changes in sensorium:
 ✧ Disturbed sleep
 ✧ Drowsiness → stupor → coma.

6- Skin rash: rose spots may appear over the trunk and extremities esp. with meningococcal septicemia.

☆ Clinical types:

1- Meningitic form: the classic presentation (see above).

2- Fulminating meningitic form:

✧ Explosive onset with high fever, severe headache and convulsions.
 ✧ Rapid progress to coma with fatal outcome within 48hrs.

3- Septicaemic form:

✧ Very bad general condition with shock.
 ✧ Marked skin manifestations with purpura.
 ✧ Meningitis may develop after 1-2 days or not develop at all.
 ✧ Usually complicating meningococcal form.

☆ Complications:

I- Peripheral circulatory complications:

- ❖ Water-House Freidrichson syndrome:
 - Adrenal hge (acute Addisonian crises).
 - Septicaemia, shock with extensive petichie & ecchymosis (purpura fulminans).
- ❖ Disseminated intravascular coagulation (DIC) with purpura, bleeding from puncture sites and gangrene of the extremities.

II- Neurological complications.

- ❖ Subdural effusion esp. with H.influenza or pneumococci.
- ❖ Hydrocephalus.
- ❖ Chronic neurological damage (Deafness, cranial nerve palsies).

III- Hematogenous dissemination:

- ❖ Arthritis
- ❖ Osteomyelitis.
- ❖ Endocarditis.

☆ Investigations:

- ❖ CBC → Leukocytosis.
- ❖ Blood culture → may be +ve for the causative bacteria.
- ❖ CSF → Done twice: the 1st for diagnosis, (C & S). The 2nd after 1 week to evaluate ttt.
 - Shows specific data (see D.D. of CSF in meningitis).
 - Should be avoided in ↑ ICT or bleeding disorders.

☆ D.D.:

1- Other causes of meningitis (see later).

2- Brain abscess.

3- Encephalitis.

4- Meningism: non infectious meningeal irritation due to extra cranial lesions e.g. pneumonia, otitis media, Which shows normal CSF.

☆ Management:

I- Prevention:

- ❖ Vaccination against H.influenza, pneumococci & meningococci (non-compulsory)
- ❖ Chemoprophylaxis for contacts: e.g. rifampicin 10-20 mg/k/day.
- ❖ Good hygiene and isolation of the case.

II- Treatment:

1- Antibiotic therapy:

- ⌚ For 2-4 weeks IV according to cultures & S.
- ⌚ While waiting for C & S the following combination is recommended:
 Penicillin G 200-300.000 unit/kg/d (vancomycin if the patient is older than 3 months)+ 3rd generation cephalosporins 200 mg/kg/d+ acyclovir (if viral etiology not excluded).

2- Supportive therapy:

- ⌚ ↓ ICT: Mannitol/Lasix/elevation of the head 30°/mechanical hyperventilation.
- ⌚ Cortecosteroids: In severely ill or shocked patients (esp. in H.inf. & pneum)
- ⌚ Treatment of Convulsions.
- ⌚ Treatment of Complications.

☆ Prognosis: Depends on:

- 1- Age: → the younger the age, the worse the prognosis.
- 2- Course: → fulminant meningitis has worse prognosis.
- 3- Cause: →
 - E.coli & Staph→↑ fatality & ↑ long term sequelae.
 - H.influenza & Pneumococci → moderate prognosis.
 - Meningococci → ↓ 5% fatality & no residual disability.

ASEPTIC MENINGITIS

☆ **Def.:**

Acute inflammation of the meninges with no bacteria in CSF either by gram-stain or on culture.

☆ **Aetiology:**

1- **Viruses:**

- Enteroviruses (Coxsackie and Echo) → commonest.
- Others e.g mumps, EBV, HSV.

2- **Miscellaneous infections:**

- Toxoplasma
- Malaria.
- \$
- Trichinosis

3- **Non-infectious causes:**

- Post vaccination (Rabies, Measles, ...)
- Intrathecal injection.
- CNS leukaemia.

☆ **Clinical manifestations:**

As septic meningitis but fever may be lower and headache is very common.

☆ **Investigations:**

1- **CSF exam:** → see later.

2- **Virological studies** → Viral isolation from CSF, stool or throat.

☆ **D.D:** As septic meningitis.

☆ **Treatment:**

Supportive and symptomatic ttt (Analgesics, Antipyretics, hospitalization and ↓ ICT)

☆ **Prognosis:**

The prognosis is generally excellent and recovery occurs in most cases within 1-2 weeks, rarely encephalitis may develop.

CSF IN MENINGITIS

Condition	Appearance	Pressure (mmH ₂ O)	Protein (mg/dl)	Glucose (mg/dl)	Leukocytes / ml	Organism
• Normal CSF	Clear	50-200	20-40	2/3 of blood glucose	0-5 (monocytes)	Nil
• Bacterial meningitis	Turbid	↑↑	↑↑ (> 100)	↓↓	↑↑ (100-60,000) PNL's predominate	* +ve Gram stain * +ve culture
• Partially treated bact. meningitis.	Turbid ± clear	↑↑	↑↑ (> 100)	N. or ↓↓	↑ (10-10,000) Early PNL's, later mononuclear cells predominate	* Organisms may or may not be detected
• TB meningitis	Web On stand	↑↑	↑↑ (> 100)	↓↓	↑ (10-500) Early PNL's. Later lymphocytes.	* Acid fast bacilli by ZN stain.
• Viral meningitis	Clear	Normal or slightly ↑	Mild ↑ (< 100)	N. or ↓↓	↑ (10-500) Early PNL's later mononuclear cells predominate	* Viruses may be isolated from CSF

X- ENCEPHALITIS

✱ **Definition** Inflammation of the brain tissues

✱ **Aetiology**

I- **Infection:**

- **Viral** → HSV, Mumps, Measles, G.Measles, Varicella, Rabies, ...
- **Fungal:** → Aspergillosis and cryptococcosis.
- **Protozoa:** → Toxoplasma and malaria.
- **Spirochetal:** → S. , Leptospirosis.

II- **Allergy:**

- **Post-infection** (Mumps, Measles, G.measles, Chicken P, Pertussis)
- **Post-vaccination** (Measles, Pertussis, Rabies,)

✱ **Clinical Picture:**

There is wide range of manifestations regarding! cause and! extent of brain damage:

- 1- Onset with fever, vomiting, headache.
- 2- Hallucination in children or screaming spells in infants.
- 3- Abnormal movements and convulsions ($\pm$ stupor and coma in severe cases).
- 4- Focal neurological lesions may occur (ocular, limb,)

✱ **Investigations:**

- ① **CSF examination:** • As aseptic meningitis
- ② **Special tests:**
 - Viral isolation from CSF, blood or throat swab or by serology
 - Tests for fungal, protozoal or spirochaetal infections.

✱ **Differential diagnosis**

- ① Meningitis esp. T.B. ② Lead encephalopathy. ③ Space occupying lesions

✱ **Complications:**

Long term sequelae of encephalitis include:

- Mental retardation.
- Epilepsy.
- Cerebral palsy.
- Auditory and visual disturbances.

✱ **Prognosis:**

- Depends on: ① Age of the patient: the younger the patient the worst the prognosis.
② The causative agent: HSV has the worst prognosis

✱ **Treatment**

- **Supportive measures:** As septic meningitis.
- **Antiviral agents:** Mainly used in HSV ($\uparrow\uparrow$ fatality) after confirming the diagnosis by temporal lobe biopsy:
 - **Vidarabine** → 15 mg/k/day continuous IV infusion for 15 days.
 - **Acyclovir** → 15 mg/k/dose I.V. in 3 doses for 15 days.

CHAPTER (VIII)

ENDOCRINE

(I) PITUITARY GLAND

* Ant. Pit. → GH, Prolactin, TSH, ACTH, LH & FSH.

* Post. Pit. → ADH & oxytocin

GROWTH HORMONE DEFICIENCY

⊛ Def.: ↓ GH either isolated or associated with ↓ other pituitary hormones.

⊛ Causes:

- 1- Idiopathic (the commonest): No demonstrable lesion of the pituitary but low GH either isolated or with other hormonal deficiency.
- 2- Deficiency of GH or GHRH: Familial.
- 3- Developmental: Aplasia or hypoplasia of the pituitary gland.
- 4- Destructive lesions: Trauma, tumours, surgery.
- 5- End organ unresponsiveness:
 - a) Insulin like growth factor-1 deficiency (IGF-1↓): IGF-1 is produced by kidney & liver in response to GH to perform the actions of GH. It may be low in (Laron syndrome → AR & African pygmies). These cases respond to treatment with (IGF-1) but not to GH.
 - b) Biologically inactive GH with normal plasma level.

⊛ Clinical Picture:

- 1- At birth: (non-destructive types):
 - Normal size with microphalus (the retarded growth appears between 2-3 years).
 - May present with neonatal emergencies (cyanosis, apnea, convulsions,.....).
- 2- Signs of ↑ ICT & other hormonal deficiency (in destructive types)
- 3- Later on: (In all types):
 - Proportionate dwarfism with normal mentality ± hypogonadism & hypoglycaemia.
 - Facial features (round head, bulging eyes, small mandible & short neck).

⊛ D.D.: other causes of short stature.

⊛ Investigations:

- 1- GH level in plasma (N. > 7 ng/ml).
Better done after stimulation of GH release e.g. 20 min. exercise or injection of provocative agents as insulin, dopamine or arginine.
- 2- Level of IGF-1 (if ↓ of IGF-1 is suspected).
- 3- Estimation of other pituitary hormones (TSH, LH, prolactin,.....).
- 4- Investigations for the cause
 - Plain x-ray skull, CT or MRI ⇒ for space occupying lesions & ↑ ICT.

⊛ Treatment:

- 1- Treatment of the cause if possible.
- 2- GH therapy (Genotropine amp.) ⇒ given S.C. injection (0.3 mg/K/week in 5-6 inj.)
- 3- Recombinant (IGF-1) in cases of IGF-1 deficiency.

SHORT STATURE

★ Def.:

Height below the 3rd centile for age & sex.

★ Classification:

- 1- Proportionate short stature: (normal US: LS and arm span / height ratio).
- 2- Disproportionate short stature: (abnormal US: LS and arm span / height ratio).

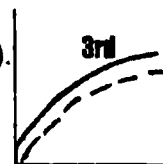
★ Causes and Manifestations:

1-PROPORTIONATE SHORT STATURE

A) Normal Variants:

★ Familial:

- Birth size is small (but normal for family).
- Normal bone age & puberty.
- Ultimate height is short (as parents).



★ Constitutional:

- Normal birth length up to 6 month then ↓ ↓ length below normal for 2-3 yrs then recatch length again.
- Delayed bone age & puberty.
- Normal adult height.



B) Pathological:

★ Chronic systemic illness:

- | | |
|---------------------------|-----------------------------------|
| • Chronic chest diseases. | • Cong. & Rh. heart diseases. |
| • Chronic renal failure. | • Chronic hemolytic anaemia. |
| • Chronic malabsorption. | • Chronic neurological disorders. |

★ Malnutrition:

- Marasmus, anorexia,

★ Maternal deprivation:

- Disturbed child / mother or family relations (psychogenic).

★ Endocrinal causes:

- | | |
|---------------------------|-------------------------------|
| • Hypopituitarism (GH ↓). | • Hypothyroidism (cretinism). |
| • Hypoparathyroidism. | • Hypercorticism (Cushing). |
| • DM. | • D I |

★ Miscellaneous causes:

- | | |
|--------------------|---------------------------|
| • Down syndrome. | • Turner syndrome. |
| • Noonan syndrome. | • Silver Russel syndrome. |

2-DISPROPORTIONATE SHORT STATURE

A) Short limbs

- Achondroplasia.
- Osteogenesis imperfecta.
- Mucopolysaccharidosis.
- Rickets.

B) Short trunk

- Morquio's Disease.
- Ectodermal dysplasias.
- Fanconi anaemia.

☆ Approach to the Diagnosis

(I) HISTORY

1- Perinatal history:

- Infection, cong. anomalies, maternal drugs in pregnancy,
- Birth weight, length & gestational age.

2- Family history:

- Height, height at childhood.
- Social problems.
- Nutritional status.

3- Past history:

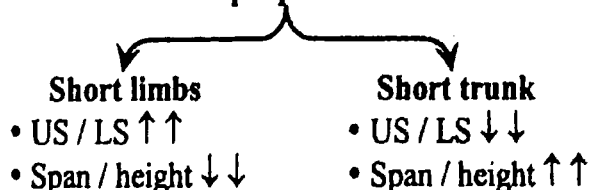
- Of systemic illness (renal, cardiac, chest,.....).
- Of endocrinal problems.

(II) EXAMINATION

⇒ Proportionate

- Exam. For systemic illness.
- Exam. For malnutrition.
- Exam. For endocrinopathies.
- Exam. For specific syndromes (dysmorphic features, associated problems,.....)

⇒ Disproportionate



N.B.:

- ① US / LS 1.7 at birth, 1.3 at 3 years & 1 at 7 years.
- ② Arm span / height = 1 (but span is 4 cm less than height below 7 years old).

(III) INVESTIGATIONS

1- Bone age (x-ray left wrist) usually retarded (normal in dysplasias & familial causes).

2- Hormonal assay (GH, T3,).

3- Karyotyping: esp. female with extreme short stature.

4- Investigations for chronic systemic illness:

- CT & MRI → to detect brain tumours or malformations.
- Anaemia → CBC
- T.B. → x-ray chest.
- Renal → urea, creatinine.
- Malabsorption → stool analysis,.....

☆ Treatment

1- Of the cause:

- Hormonal replacement esp. GH (discuss).
- Treatment of renal, heart, GIT, problems.
- Treatment of rickets.

2- Supportive measures

- Good nutrition + minerals & vitamins.
- Psychological support in maternal deprivation.

GROWTH HORMONE EXCESS

- * **Def.:** ↑ GH leads to:
 - Gigantism (before closure of epiphysis).
 - Acromegaly (after closure of epiphysis).
- * **Causes:**
 - 1- Pituitary adenoma.
 - 2- ↑ GHRH by hypothalamic or pancreatic tumours.
- * **C/P:**
 - 1- Gigantism (rapid linear growth) ⇒ tall stature.
 - 2- Acromegaly (enlargement of distal parts of the body).
- * **D.D.:** Other causes of tall stature.
- * **Investigations:**
 - 1- Hormonal profile: ↑ GH & ↑ IGF-1 (± ↑ GHRH).
 - 2- CT & MRI to detect tumours.
- * **Treatment:**
 - 1- Medical → Bromocriptine OR Octreotide
 - 2- Surgical treatment or irradiation for the tumours.

TALL STATURE

- * **Def.:** Height more than the 97th centile for age & sex.
- * **Causes:**

<u>A) Proportionate</u>	<u>B) Disproportionate</u>
• Familial	• Marfan syndrome (AD)
• Simple obesity.	• Homocystinuria (AR)
• GH excess (gigantism).	• Soto syndrome (AD)
• Hyperthyroidism.	• Klienfelter syndrome (XXY male)

DIABETES INSIPIDUS (DI)

- * **Def.:** Defective water reabsorption 2ry to decrease ADH level or its action.
- * **Causes:**
 - 1- **Central DI** (↓ synthesis of ADH)
 - a) Hereditary: AD OR AR ⇒ DIDMOD (Wolfram syndrome)
 - b) Acquired:
 - Destructive lesion at neurohypophysis (post. pit. / hypothalamic junction) by tumours, trauma, operations or encephalitis.
 - Idiopathic ⇒ must be followed up by CT brain for 4 years as a lot of idiopathic cases may be due to small undetected brain tumours.
 - 2- **Nephrogenic DI** (End organ unresponsiveness)
 - a) Hereditary: X-linked recessive.
 - b) Acquired: e.g. hypercalcaemia, hypokalaemia, renal failure, urinary obstruction & interstitial nephritis.

* **C/P:**

- 1- Polyuria & polydipsia.
- 2- Episodes of dehydration, fever and shock.
- 3- Growth failure and anorexia.
- 4- Manifestations of the cause (e.g. $\uparrow$ ICT in brain tumours).

* **Investigations**

(I) To prove DI:

1- **Urine:**

- $\uparrow$ volume (4-10 litres / day).
- $\downarrow$ specific gravity (1001 – 1005) and fail to rise above 1010 even with fluid restriction.

2- **Water deprivation test:**

- Restriction of water intake for 8 hours (marked $\uparrow$ plasma osmolarity but urine volume remains $\uparrow$ and urine osmolarity remains low).

(II) To differentiate nephrogenic from central DI:

1- **ADH serum level:**

- Low in central DI.
- Normal or high in nephrogenic DI.

2- **Response to desmopressin (synthetic ADH analogue):**

- Improvement occurs only in central DI.

(III) Investigations for the cause:

1- **In central DI:** X-ray, CT or MRI skull.

2- **In nephrogenic DI:**

- Urine analysis.
- KFT
- Serum electrolytes.
- Abdominal ultrasound.

* **D.D.:**

1- **DI must be differentiated from other causes of polyuria & polydipsia:**

- Endocrinal $\Rightarrow$ DI & DM.
- Metabolic $\Rightarrow$ hypercalcaemia, hypokalaemia & CRF.
- Tumours $\Rightarrow$ pheochromocytoma & neuroblastoma.
- Psychogenic polydipsia.
- Ingestion of diuretics or excess tea, coffee, beer,

2- **Nephrogenic DI must be differentiated from central DI.**

* **Treatment:**

1- **Treatment of the cause** if 2ry.

2- **Adequate hydration** and correction of electrolyte imbalance.

3- **In central DI:** Desmopressin 10-15 μ g/day by nasal inhalation.

4- **In nephrogenic DI:**

- Diuretics ($\uparrow$ Na loss $\rightarrow$ stimulate the kidney to reabsorb Na $\rightarrow$ Na & H₂O retention) $\Rightarrow$ paradoxical effect of diuretics.
- Indomethacin (anti-PG) in resistant cases.

(II) THYROID GLAND

PHYSIOLOGICAL CONSIDERATION

* **Synthesis of thyroid hormones:**

- 1- Trapping: thyroid uptake of iodide.
- 2- Oxidation of iodide to iodine
- 3- Iodine + tyrosine $\rightarrow$ MIT or DIT
- 4- Coupling: DIT + DIT $\rightarrow$ T₄.
DIT + MIT $\rightarrow$ T₃.

* **Regulation of thyroid hormones:**

- Hypothalamus (TRH $\rightarrow$ + + TSH).
- Ant. Pituitary (TSH $\rightarrow$ + + T₃, T₄).
- Thyroid gland ($\uparrow$ T₃, T₄ $\rightarrow$ - - TRH & TSH).

* **Thyroid function tests:**

1- **Non-specific tests:**

- Sleeping pulse rate $\rightarrow$ $\downarrow$ in hypo. & $\uparrow$ in hyper.
- BMR $\rightarrow$ $\downarrow$ in hypo & $\uparrow$ in hyper.
- Serum cholesterol $\rightarrow$ $\uparrow$ in hypo & $\downarrow$ in hyper.

2- **Specific tests: (serum)**

- TSH $\rightarrow$ $\uparrow$ (hypoth.) & $\downarrow$ (hyperth. OR hypo due to hypothalamic defect).
- T₃, T₄ level $\rightarrow$ $\uparrow$ (hyper) & $\downarrow$ (hypo).
- Free T₄ level $\rightarrow$ $\uparrow$ (hyper) & $\downarrow$ (hypo).
- Protein binding iodine (PBI) $\rightarrow$ $\uparrow$ (hyper) & $\downarrow$ (hypo).
- T₃ resin uptake $\uparrow$ (hyper) & $\downarrow$ (hypo).
- Free thyroxin index PBI $\times$ T₃ resin uptake $\uparrow$ (hyper) & $\downarrow$ (hypo).

N.B.: T₄ is more sensitive than T₃ as T₃ may be $\uparrow$ by peripheral conversion of T₄

HYPOTHYROIDISM

(I) CONGENITAL HYPOTHYROIDISM "Cretinism"

* **Aetiology:**

- 1- **Hypothalamic defect** ($\downarrow$ TRH) $\rightarrow$ tertiary hypothyroidism.
- 2- **Pituitary defect** ($\downarrow$ TSH) $\rightarrow$ secondary hypothyroidism.
- 3- **Thyroid defect** ($\downarrow$ T₃, T₄) $\rightarrow$ primary hypothyroidism.
 - Aplasia, hypoplasia or ectopia of the thyroid gland (90 % of cases).
 - Dyshormonogenesis: due to defective synthesis of thyroid hormones or maternal antithyroid drug intake during pregnancy.
 - Endemic cretinism (iodine deficiency of the mother during pregnancy).
- 4- **End organ unresponsiveness:**
 - TSH unresponsiveness
 - Thyroid hormone unresponsiveness

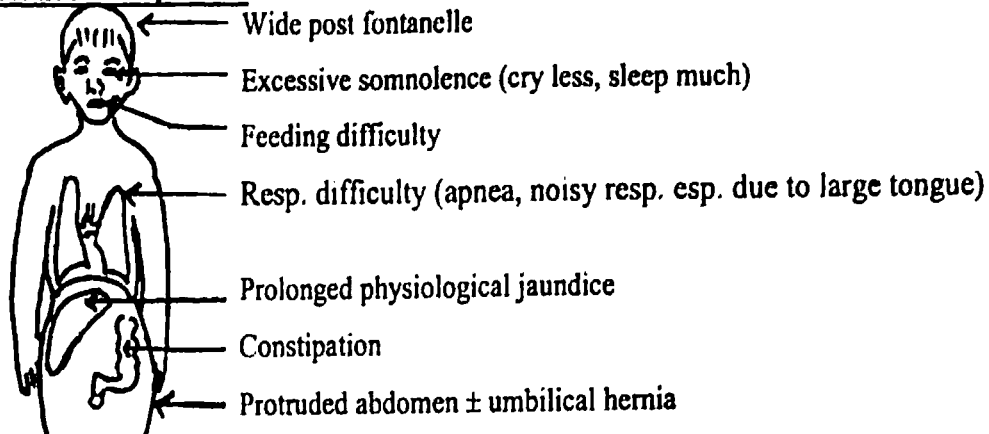
} Receptor defect

* **Incidence:**

- 1: 4000 live births.
- Female: Male 2 : 1.

* C/P:1) At birth:

- The baby may be heavier than normal (due to myxoedema of the brain).

2) In neonatal period:3) With growth:

- Delayed motor development (head support, sitting,).
- Delayed mental development (social, speech,.....).

4) Full picture of cretinism: (by the end of the first year).a) Delayed motor milestonesb) Delayed mental milestones (MR)c) Delayed growth: with chch short stature and persistence of infantile proportions.d) Delayed sexual maturation (in severe cases precocious puberty !!).e) Physical features:

- ↳ Head : Slightly ↑ H.C. + delayed closure, wide AF.
- ↳ Hair : Coarse, scanty with low anterior hair line.
- ↳ Eyes : Hypertelorism, puffy with narrow palpebral fissure.
- ↳ Nose : Broad nostrils & depressed nasal bridge.
- ↳ Mouth : Large protruded tongue with delayed teething & pallor.
- ↳ Neck : Short neck with supraclavicular fat deposition.
- ↳ Thyroid : Large in dyshormonogenesis and some cases of endemic cretinism.
- ↳ Muscle : Hypotonia rarely pseudohypertrophy (Kocher, Debre Semelaigne).
- ↳ Skin : Myxedematous deposits ± yellow colour (carotein deposition).
- ↳ Hands : Short, broad, cold, dry.
- ↳ Abdomen : Protruded with constipation ± umbilical hernia.
- ↳ Others : ♣ Hypothermia ♣ Hypotonia
 ♣ Slow pulse ♣ Slow respiration

* Investigations:1- Thyroid function tests (see before)2- Radiological:• X-ray bone:

- ↳ X-ray Wrist : Delayed bone age.
- ↳ X-ray Knee: Absent tibial & femoral epiphysis.
- ↳ X-ray Spine: Beaking (deformity) of T12, L1.

• X-ray skull:

- ↳ Macrocephally, large fontanelles ± intrasutural bone (wormian skull).
- ↳ Evidences of ↑ ICT in pit. tumours.

- Thyroid scanning to detect thyroid aplasia or ectopy and study thyroid function.

* **D.D.:**1- **Other causes of mental & growth retardation:**

- Mongolism and other chromosomal anomalies.
- Mucopolysaccharidosis

2- **If enlarged thyroid it must be D.D. from other causes of goitre (thyroid enlargement)**a) **Goitre with hypothyroidism:**

- ✦ Pendred syndrome (AR with deafness).
- ✦ Dysmorphogenesis.
- ✦ Endemic cretinism (some cases).
- ✦ Thyroiditis (some cases).

Causes of hypothyroidism with deafness:

- 1- Pendred syndrome.
- 2- Endemic cretinism.
- 3- Neglected hypothyroidism
- 4- Congenital Rubella syndrome.

b) **Goitre with hyperthyroidism.**

- ✦ Grave's disease.
- ✦ Thyroiditis (some cases).

c) **Goitre with euthyroid:**

- ✦ Simple colloid goitre.
- ✦ Thyroiditis (some cases).

* **Diagnosis & Prognosis:**1- **High incidence of suspicion** is required for early diagnosis of hypothyroidism from the few presenting features as delayed diagnosis is catastrophe:

- Diagnosis & treatment before 3 months → good mentality.
- Diagnosis & treatment 3-6 months → variable response.
- Diagnosis & treatment after 6 months → permanent MR.

2- **As diagnosis of hypothyroidism is difficult** in the first 3 months, screening for thyroid function is done for all neonates in the first week of life (in Egypt).* **Treatment:**

- Replacement therapy with **sodium L. thyroxine** (eltroxin 50 ug tab.) for life.

• **Dose:**

✦ Neonates	10	µg / K / d	} The dose is adjusted according to the response
✦ Infants	6 - 8	µg / K / d	
✦ Children	4	µg / K / d	
✦ Adults	2	µg / K / d	

• **Follow up:**

- ✦ Clinically by ↑ activity, improvement of constipation, milestones & growth.
- ✦ Laboratory by normal T₄, TSH (T₃ is not a reliable marker. Why?).
- ✦ Radiologically by ossific centers & bone age.

- **Side effects:** In high doses manifestations of hyperthyroidism may occur.

* **N.B.: Endemic cretinism:**

- ⊗ Neonatal hypothyroidism results from marked maternal iodine intake deficiency during pregnancy in endemic areas (e.g. Guinea, Zair,.....).

- ⊗ It has 2 types:

♥ **Neurological type**

- ☆ Goitre
- ☆ Early hypothyroid then euthyroid.
- ☆ Mental affection.
- ☆ Minimal or no physical retardation.

♥ **Myxedematous type**

- ☆ Thyroid atrophy.
- ☆ Permanent hypothyroidism.
- ☆ Mental affection.
- ☆ Severe physical retardation.

- ⊗ Single dose of iodinated poppy seed I.M. to females living in endemic areas is sufficient as a prophylaxis for up to 5 years.

(II) ACQUIRED HYPOTHYROIDISM

"Juvenile hypothyroidism"

* Aetiology:

- 1- Injury to the thyroid gland: trauma, surgery, irradiation
- 2- Infiltration of the thyroid gland: hemochromatosis, tumours.
- 3- Iodine containing drugs: e.g. cough mixtures & amiodarone.
- 4- Inflammation (thyroiditis) → the most common cause.
 - a) Hashimoto (lymphocytic) thyroiditis: autoimmune dis. with goitre (the commonest)
 - b) Acute suppurative thyroiditis: due to bacterial infection.
 - c) Subacute non-suppurative thyroiditis: due to viral infection.
 - d) Chronic thyroiditis: due to T.B & sarcoidosis.

N.B: All types of thyroiditis may be associated with normal, hypo or hyperthyroidism.

* C / P:

- 1- Features of the cause.
- 2- Mental: Apathy, sleepiness & school underachievement (but no MR).
- 3- Sexual: Delayed puberty (may be early ??).
- 4- Physical: Deceleration of growth, constipation, myxoedematous thickening of skin with cold peripheries.

* Investigations & Treatment: As cong. hypothyroidism .

- Thyroid antiperoxidase antibodies , Thyrotropin receptor blocking antibodies in suspected autoimmune thyroiditis.

HYPERTHYROIDISM ⇒ uncommon

* Aetiology:

1- 1ry hyperthyroidism (Grave's disease):

- Autoimmune disease (antibodies which stimulate thyroid secretion).
- Associated with exophthalmos, goitre and other autoimmune diseases.

2- 2ry hyperthyroidism

- Thyroiditis (some cases).
- Nodular toxic goitre.
- Functioning cancer thyroid.

3- Congenital hyperthyroidism

Due to transplacental passage of antibodies from mother with Grave's disease to the fetus.

* C / P: Exaggerated functions of thyroxin e.g.:

- ① CVS → Tachycardia, arrhythmia & water – hammer pulse.
- ② CNS → Hyperreflexia, irritability & tremors.
- ③ GIT → Progressive Wt. Loss (despite good appetite).
- ④ In Grave's disease → Associated exophthalmos or goitre.

* Investigations:

- 1- Thyroid function tests: → see before.
- 2- For the cause (antibodies in Grave's dis., thyroid scan for tumours,.....).

* Treatment:

- 1- Medical → Antithyroid drugs (carbimazol) + Inderal.
- 2- Surgical → If failed medical treatment (subtotal thyroidectomy).

(III) PANCREASE

- * The pancreas has two functions:
 - ① Exocrine functions → digestive enzymes.
 - ② Endocrine function through 2 hormones insulin (from β -cells) & glucagon (from α -cells).
 - Insulin → ↓ blood glucose level.
 - Glucagon + others (Adrenaline, cortisone) → ↑ blood glucose level.

DIABETES MELLITUS

- * **Def.:** Chronic metabolic disorder caused by deficiency of insulin or its action, manifested by abnormal metabolism of CHO, ptn. and fat.
- * **Classification:** (Normal plasma glucose $\leq$ 120 mg/dl → fasting and $<$ 140 mg/dl post glucose load).
 - 1- **Type (I) (Insulin dependent DM)** → (juvenile onset DM).
The main type in Pediatrics, chch by random plasma glucose $>$ 200 mg/dl + typical features of DM.
 - 2- **Type (II) (Non-IDDM)** → (adult onset DM).
Uncommon in Pediatrics, chch by fasting plasma glucose $>$ 126 mg/dl + 2 hrs post glucose load $>$ 200 in more than one occasion.
 - 3- **2ry DM:** → (Either IDDM or non-IDDM)
Due to syndromes (Turner, Prader-Willi,...), drugs (steroids,...) or pancreatic diseases (cystic fibrosis, hemochromatosis,...).
 - 4- **Impaired glucose tolerance:**
 - Fasting plasma glucose $<$ 140 mg/dl.
 - 2 hrs post prandial glucose $>$ 140 mg/dl.
 - 5- **Gestational diabetes:**
 - Features of DM in pregnant female who was non-diabetic before pregnancy.
- * **Aetiology of IDDM:** (Multifactorial)
 - 1- **Genetic predisposition:**
Higher incidence of IDDM is observed in people with HLA-DR3 & HLA-DR4.
 - 2- **Autoimmune response:**
 - Evidences:
 - ↳ Presence of antibodies against islet cells (80%).
 - ↳ Association of IDDM with autoimmune diseases in some cases.
 - 3- **Environmental factors:**
Viral infection (e.g. measles, mumps, rubella, EBV) can initiate IDDM in genetically predisposed individuals.
- * **Pathophysiology of IDDM:**
 - (I) **The main functions of insulin are:**
 - 1- ↓ blood glucose by:
 - ↓ gluconeogenesis. • ↓ glycogenolysis. • ↑ uptake of glucose by the cells.
 - 2- Inhibit fat breakdown (↓ lipolysis).
 - 3- Inhibit protein breakdown (↓ proteolysis).

(II) Insulin deficiency will lead to:

- 1- **Hyperglycaemia** → ↑ glucose in blood above renal threshold (180 mg/dl) → osmotic diuresis → polyuria → dehydration and compensatory polydipsia.
- 2- ↑ **proteolysis** → loss of weight & polyphagia.
- 3- ↑ **lipolysis** → ↑ free fatty acids with accumulation of acetyl Co-A → liver → keton bodies (ketonaemia, ketonuria and metabolic acidosis).

*** Manifestations of IDDM:** (IDDM has various presentations)

- 1- Polyuria, polydipsia, polyphagia and loss of weight.
- 2- 2ry nocturnal enuresis (due to polyuria ± UTI).
- 3- Insidious onset of vomiting, lethargy and abdominal pain.
- 4- Recurrent skin infection (or vulvo-vaginitis in female).
- 5- Diabetic ketoacidosis is the presenting feature in about 10-20 % of newly discovered patients with IDDM.

*** Investigations of IDDM:**

- 1- **Urine:** glucosuria ± ketonuria (in DKA).
- 2- **Blood glucose:** fasting > 140 mg/dl & random > 200 mg/dl.
- 3- **Glucose tolerance test:** diabetic curve.
- 4- **Glycosylated Hb (Hb A1C) level:**
 - Formed by irreversible reaction between globin chain & glucose.
 - Estimates diabetic control in the last 2-3 months:
 - ↳ If (5 – 8 %) of Hb → good control.
 - ↳ If (> 10 %) of Hb → poor control.

*** Treatment of IDDM:**

= Life long management of diabetic ketoacidosis → see page 303.

*** Complications of IDDM:****1- Acute complications:**

- **Coma:**
 - ↳ Hypoglycaemic coma (↑ insulin).
 - ↳ Diabetic ketoacidosis.
 - ↳ Hyperglycaemic - hyperosmolar non ketotic coma (HHNK).
- **Cerebral oedema** (hyperosmolarity & iatrogenic).
- **Cardiac arrhythmias** (hyper and hypokalaemia).

2- Chronic complications:

- Delayed growth.
- Diabetic angiopathy (nephropathy, neuropathy & retinopathy).
- Defective immunity (recurrent infection).

3- Complications of treatment (insulin):

- Local reaction (lipoatrophy or lipohypertrophy).
- Hypoglycaemia.
- Hypersensitivity (treated by change to human insulin).
- Insulin resistance (usually due to insulin antibodies treated by ↑ insulin dose).

MANAGEMENT OF DIABETIC KETOACIDOSIS

* Diagnosis of DKA

1- History:

Of the precipitating factor, DKA is usually precipitated by infection, stress or vomiting.

2- Clinical manifestations:

- **Early:** Polyuria, vomiting, abdominal pain $\pm$ fever (infection or dehydration).
- **Next:** Dehydration, acidotic (deep, rapid) breathing $\pm$ acetone odour of breath.
- **Late:** Shock and coma.

3- Investigations:

- **Diabetic** $\rightarrow$: Blood glucose > 300 mg/dl + Glucosuria.
- **Keto** $\rightarrow$: Keton bodies in serum > 3 m Mol/L + Ketonuria.
- **Acidosis** $\rightarrow$: Metabolic acidosis ($\downarrow$ pH, $\downarrow$ PaCO₂, $\downarrow$ HCO₃) in ABG's.

4- D.D.: From other causes of diabetic coma:

- **DKA:** $\uparrow$ blood glucose + ketonaemia & ketonuria.
- **HHNK:** $\uparrow$ blood glucose without ketonaemia or ketonuria
(Uncommon, associated with severe dehydration & high fatality).
- **Hypoglycaemia:** $\downarrow$ blood glucose + manifestations of hypoglycaemia.

* Treatment of DKA

① During the acidotic phase

A) Preparations:

- Hospitalization (better in the ICU).
- O₂ + nasogastric suction.
- Insertion of 2 I.V. lines (one for insulin and one for fluid therapy).
- Monitoring of vital signs, fluid intake, urine output & blood glucose (every 1-2 hrs).

B) Correction of dehydration & shock:

- Shock therapy 20-30 ml / Kg $\rightarrow$ saline or ringer lactate over one hour. THEN
- Deficit therapy 70-100 ml/Kg + maintenance therapy 100 ml/kg (both are mixed together and given over 24 hours $\rightarrow$ $\frac{1}{2}$ the amount in 8 hours then $\frac{1}{2}$ the amount in 16 hours.
- The fluid therapy is given in the form of normal saline (0.9%) till blood glucose falls below 300 mg/dl then change of fluid therapy to Saline: Glucose 5% (1 : 1) then gradual $\uparrow$ of glucose with improvement of DKA.
- K⁺ is added to the fluids (1.5 ml KCl for each 100 ml fluids) 1-2 hours after initiation of insulin therapy irrespective to serum potassium level (Why?).

C) Correction of metabolic acidosis:

- Only severe acidosis (PH < 7.15) will be corrected by NaHCO₃ (1-2 ml/Kg) & mild acidosis will be self limited.

D) Correction of hyperglycaemia (Insulin therapy): (less urgent than tit of shock)

- Continuous low dose infusion of regular insulin: Initially 0.1 U/Kg bolus IV followed by 0.1 U/Kg/hour IV infusion.
- When blood glucose falls below 300 mg/dl previous method stopped and replaced by S.C. injection of 0.2-0.4 U/kg short acting insulin every 6 hours.

E) Correction of the precipitating factor:

e.g. infection by broad spectrum antibiotics.

② During post-acidotic phase**A) Initiation of oral feeding:**

- Start with small amount of water.
- If no vomiting, soft diet (skimmed milk, fruit juices) can be given every 3-4 hours.
- After 1-2 days usual diet is gradually added.

B) Insulin therapy:

- Short acting (regular) insulin is given S.C. at a dose of 0.2-0.4 U/Kg every 6-8 hours ½ hour before meal with monitoring of blood glucose before meal and 2 hours after meal.
- The dose of insulin is ↑ or ↓ according to the response.

C) Follow up:

- By blood & urine glucose (urine must be glucose free).
- Hypoglycaemia is dangerous so it's better to keep blood glucose slightly above normal (100 – 180 mg/dl).
- At the end of this stage the total daily dose of insulin is calculated to be a guide for the life long management.

③ Life-long management (= treatment of DM)**A) Diet:**

- The same total caloric intake as usual in normal child is given with the same ratios (50% CHO, 35% fat & 15% protein).
- CHO is given in complex form (starchy products, fruits) but refined sugars, sweets and carbonated beverages should be avoided.
- Number of meals is preferred to be 3 fixed major meals with 2 snacks inbetween.
- In severe exercise give excess sugars or reduce the insulin dose.

B) Insulin therapy: (Either Pork or Human Source)

According to calculated dose in post acidotic phase or can be calculated as following:

Age in years	Dose (U/Kg/day)
0-5	0.6-0.7
5-12	0.7-1
12-18	1-1.2

♣ Types of insulin:

- Short acting (regular): Onset 1 hour, duration 6 – 8 hours e.g. actrapid.
- Intermediate acting: onset 2 hours, duration 8 – 12 hours e.g. NPH, lantarad.
- Long acting → not used in children.

♣ **Regimens of therapy:**

- The best method in children is mixture of regular insulin ($1/3^{\text{rd}}$ of the dose) and NPH ($2/3^{\text{rd}}$ of the dose) $\Rightarrow$ $2/3$ before breakfast and $1/3$ before the evening meal.
- One injection per day (Not recommended in children).
- Recently insulin pump (under trials).

C) Follow up:

♣ **General**

- General health – physical, mental & sexual maturation.

♣ **Control of diabetes:**

- Daily monitoring of urine for glucose (by strips).
- Monitoring of blood glucose (by strips or device).
- Glycosylated Hb every few months.

D) Health Education:

- Of parents (and old children) about the disease & its complications and learn them how to give the injections.

E) Special considerations:

1- Honey moon period:

- Residual function of β -cells in pancreas may be manifested by hypoglycaemia which occurs after control of recently diagnosed diabetics.
- Treatment by temporary $\downarrow$ of insulin dose.

2- Somogyi phenomenon:

- In child with high dose of insulin (> 2 U/K/day) in the form of late night (3-4 A.M.) hypoglycaemia $\Rightarrow$ Stimulation of counter regulatory hormones. $\Rightarrow$ Early morning (7-8 A.M.) hyperglycaemia.
- Treatment by $\downarrow$ the dose of night intermediate insulin.

3- Dawn phenomenon:

- In child with normal dose of insulin late night normoglycaemia but counter – regulatory hormones may normally $\uparrow\uparrow$ leading to early morning hyperglycaemia.
- Treatment by $\uparrow$ the dose of night intermediate insulin.

4- Management during infection:

- Infection may precipitate hyperglycaemia or DKA.
- Mild infection should be treated $+\uparrow$ insulin dose by 10-15%.
- Severe infection necessitates hospitalization.

HYPOGLYCAEMIA

* **Def.:**

Blood glucose < 40 – 50 mg/dl at any age.

* **Causes:**

1- **Hormonal:**

- ↑ insulin (pancreatic tumours or iatrogenic).
- ↓ counter – regulatory hormones (GH, cortisol,.....).

2- **Caloric:**

- ↓ intake (starvation, malnutrition).
- ↑ utilization (severe exercise, cold weather).

3- **Metabolic:**

- Galactosaemia, glycogen storage diseases.

4- **Drugs:**

- Insulin, inderal & salicylate poisoning.

5- **Ketotic Hypoglycaemia:**

- Hypoglycemia + Keton bodies (esp. in starvation).

* **C/P:**

1- **Manifestations of cerebral glucopenia:**

- Headache, hunger, ↓ concentration.
- Convulsions → confusion → coma.

2- **Manifestations of ↑ adrenaline release (compensatory):**

- Sweating, nausea, vomiting. • Pallor, palpitation, tremors.

* **Investigations:**

1- **To prove hypoglycaemia** (↓ blood glucose < 40 mg/dl)

2- **For the cause:** e.g. hormonal levels, metabolic screen, urine analysis,.....

* **Treatment:**

- 1- Oral or I.V. **glucose** 2- If no response → **glucagon** I.M. 3- TTT of the **cause**.

CORTECOSTEROIDS IN PEDIATRICS

* **Uses of steroid therapy in Pediatrics:**

1- **Renal:** • Nephrotic syndrome.

2- **Chest:**

- Bronchial asthma. • Certain cases of T.B.
- Acute bronchiolitis. • Some cases of stridor.

3- **Hematology:**

- Autoimmune hemolytic anaemia. • Aplastic anaemia.
- Congenital pure red cell anaemia. • Idiopathic thrombocytopenic purpura.

4- **Hepatology:** • Chronic active hepatitis.

5- **CNS:** • ↑ ICT • Certain cases of meningitis

6- **Cardiology:**

- Rheumatic fever. • Certain cases of infective endocarditis.

7- **Oncology:** • Additive to chemotherapy.

8- **Collagen:** • Rheumatoid arthritis. • SLE.

9- **GIT:** • Inflammatory bowel diseases.

10- **Endocrine:** • Adrenocortical insufficiency (Absolute indication).

CHAPTER (XVII)

PEDIATRIC EMERGENCY

Pediatric Basic Life Support

- ♦ Basic life support (BLS) is the maneuvers and skills that, without the use of technical adjuncts, permit recognition of a person in cardiac or respiratory arrest and enable the rescuer to "buy time" until the victim can receive more advanced treatment
- ♦ BLS must be initiated as rapidly as possible. Its main objective is to achieve oxygenation that "protects" the brain and other vital organs.

Pediatrics BLS Sequence

safety
stimulate
shout for assistance
Airway
Breathing
Circulation
Reassess

1. Safety

- ♦ In out-of-hospital emergencies, the rescuers should first ensure their own safety and then proceed to ensure the victim's safety.

2. Stimulate

It is important to establish the responsiveness of the collapsed child as they may not be in a critical condition.

- ⇒ If the child responds by moving, crying or talking, there may be no need for further interventions.
- ⇒ If the child does not respond, the rescuer must continue with the next steps of BLS as described below.

3. Shout

Shout out for "help" while remaining with the child.

- ♦ If there is another person available to alert the emergency medical services (EMS) team, the rescuer must ensure that the individual is capable of providing the following informations
 - ⇒ Detailed location of the emergency.
 - ⇒ Telephone number from where the call is made.
 - ⇒ Type of accident or event (infant found in cardiac arrest while sleeping, electric burn, car accident).
 - ⇒ Number and age of victims involved.

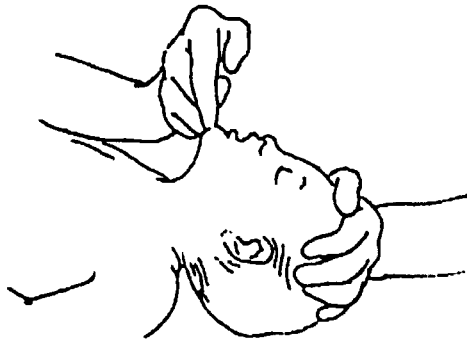
4. Airway

*** Opening the airway**

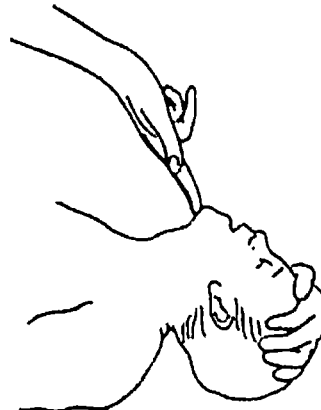
In the unconscious child, the tongue is likely to at least partly occlude the airway. Therefore, the rescuer must first open the airway as first maneuver. This can be done in two ways:

Head tilt-chin lift

This is a simple and effective maneuver indicated in all cases, except when cervical trauma is suspected.



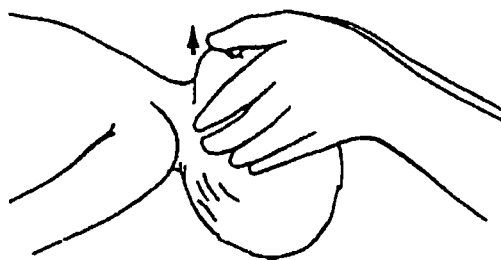
Chin lift in infants



Chin lift in children

Jaw-Thrust maneuver

This is the airway-opening maneuver of choice in all instance of suspected neck injury.



Jaw thrust

*** Checking the airway**

Whichever method of airway opening is adopted it is important to look into the mouth to ensure there is no obvious foreign body present. The rescuer should insert his fingers into the mouth only if there is a visible foreign body that the rescuer is confident that it can be removed easily.

5. Breathing

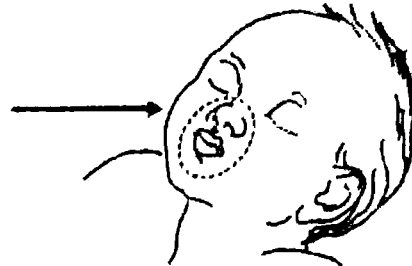
Check breathing: Look, Listen, Feel

To do this, the rescuer should position their cheek a few centimeters above the mouth and nose, whilst they look along the child's body. In this position, they can look for the rise and fall of chest and abdomen, listen for breath sounds and feel on their cheek for any air movement. They should take up to 10 seconds to look, listen & feel for breathing.

- **If the child is breathing spontaneously and effectively**, the rescuer should continue to maintain the child's airway and seek more assistance.
- **If the child has no detectable, spontaneous, effective breathing**, rescuer breaths must be delivered.

Mouth-to-mouth and nose technique

This is the method recommended to infants.



Mouth-to-mouth technique

In children, it is recommended

Once the initial rescuer breaths have been delivered, the rescuer should move onto the next step, circulation.

6. Circulation

Assess for signs of circulation

The recommended sites for assessing the central circulation is the brachial or femoral pulse in infants and the carotid artery in children.

- **If pulse is found or there are signs of circulation**, the rescue should reassess breathing.
- **If signs of circulation are absent** (no pulses and/or no signs of movement), or if the pulse is very slow (less than 60 beats/min) with signs of poor perfusion, external chest compressions (ECC) must be commenced.

Principles of external chest compressions

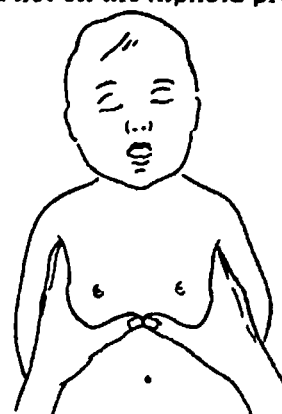
- ♦ Chest compressions are serial, rhythmic compressions of the anterior chest wall that cause blood to flow to the vital organs in an attempt to keep these organs viable until a spontaneous circulation can be restored.
- ♦ There are several effective techniques of chest compressions, but in all cases, the objective is to depress the chest one half to one third of its antro-posterior diameter.

Infant ECC

The rescuer's fingers are on the lower sternum and not on the xiphoid process.



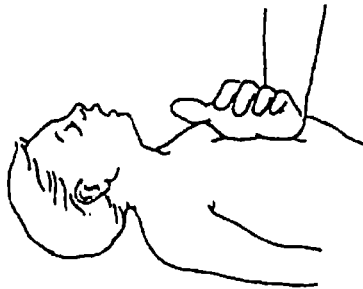
Infant ECC two finger



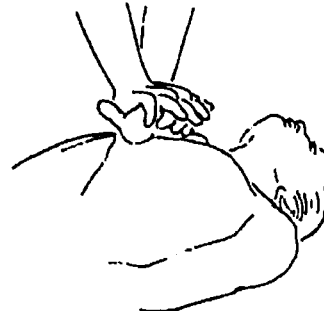
Infant ECC hand-encircling

Child ECC

The landmark for the delivery of chest compressions in the child of approximately 1-8 years is one finger breadth above the xiphoid process.



ECC in small children



ECC in older children

Compression ventilation ratio

Chest compressions should always be accompanied by rescuer breathing.

- ♦ In the infant and child, a compression-ventilation ratio of 5:1 is indicated.
- ♦ In newly-borns, more emphasis is placed on ventilation and a 3:1 compression-ventilation ratio is recommended with a maximum depth of one third of the depth of the chest.

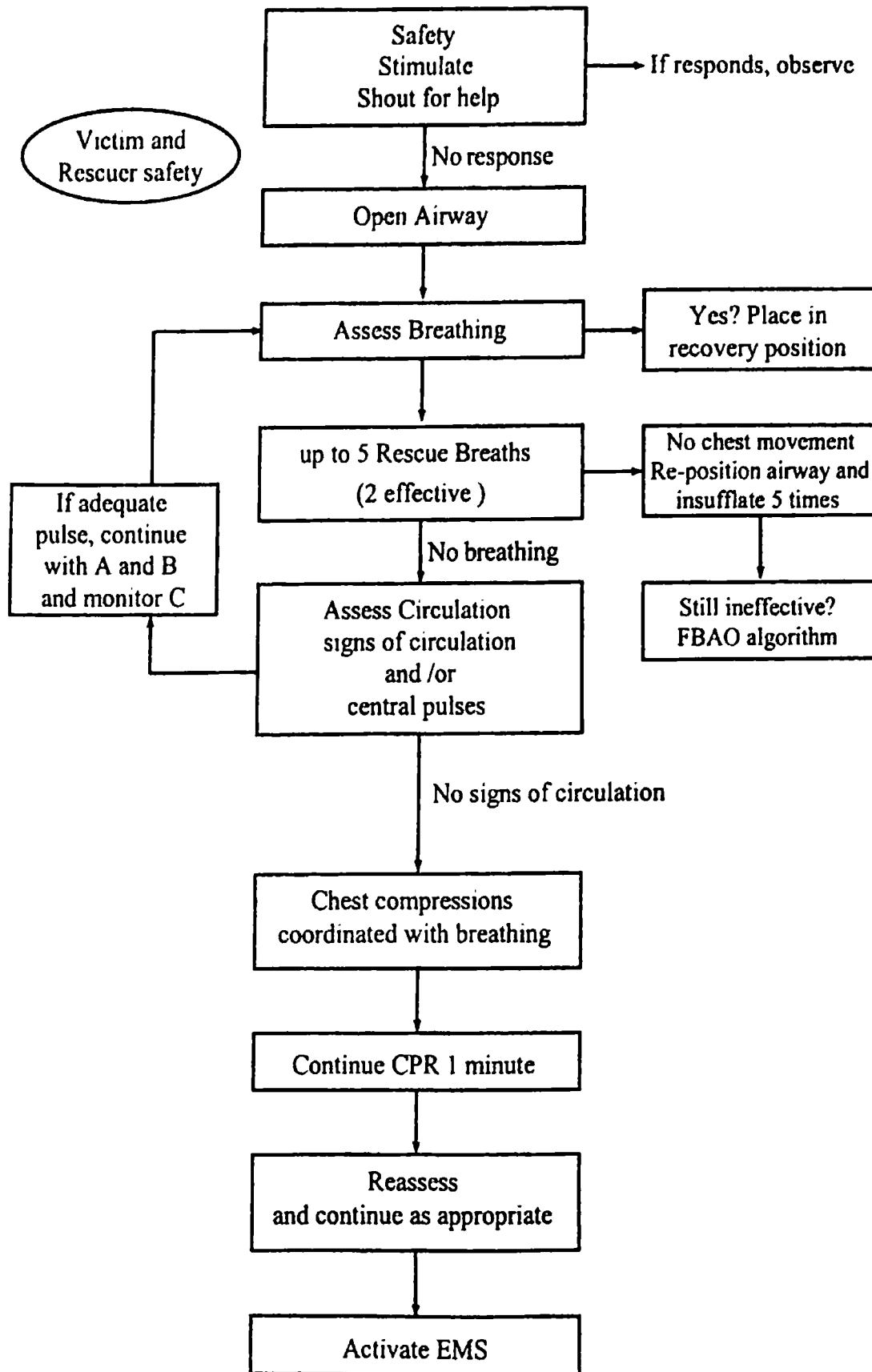
7. Reassessment

- ♥ Chest compression must be adequate to produce a palpable pulse during resuscitation. If compressions are effective, they should produce a palpable pulse in a central artery (e.g. carotid, brachial or femoral).
- ♥ After one minute of cardiopulmonary resuscitation (CPR), the rescuer should briefly stop to reassess the ABC, and also ensure that the EMS team has been summoned.

Duration of CPR

CPR should not be stopped until one of the conditions below is met:

- The child exhibits signs of spontaneous ventilation and circulation.
- A qualified healthcare team arrives to take over resuscitation.
- The rescuer becomes too exhausted to continue.



Foreign body airway obstruction

Foreign body airway obstruction

More than 90% of deaths occur in children under 5 years of age from foreign body airway obstruction (FBAO).

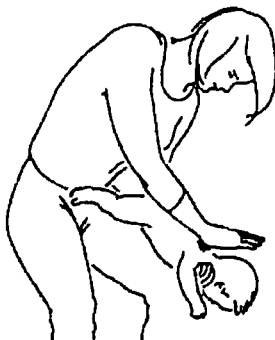
If the child is breathing spontaneously, his efforts to clear the obstruction should be encouraged with coughing and perhaps assisted by simply putting them on the back. Cough is a physiological and very effective mechanism to relieve foreign-body airway obstruction (FBAO).

☞ FBAO relief in the responsive infant

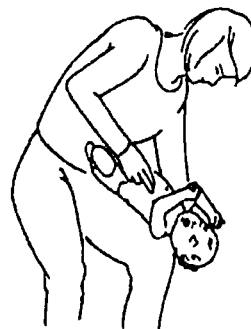
- a. Back blows.
- b. Chest thrusts.
- c. Reassess.

☞ FBAO relief in the unresponsive / unconscious infant

1. safety.
2. stimulate
3. shout.
4. Airway-open & check for easily removable foreign body.
5. Breathing – assess & have 5 attempts to deliver at least 2 effective rescuer breaths.
If ineffective, despite repositioning of the head:
6. Perform up to 5 back blows.
7. Perform up to 5 chest thrusts.
8. Airway-open & check for easily removable foreign body.
9. Breathing-assess & have up to 5 attempts to deliver at least 2 effective rescuer breaths.
If ineffective, continue with steps 6-9.
- Once attempts at rescue breaths are effective, continue with the rest of the infant BLS sequence.



Back blows in infant



Chest thrusts in infant

✧ **FBAO relief in the responsive child**

- a. Back blows.
- b. Abdominal thrusts (Heimlich maneuver).
- c. Reassess.

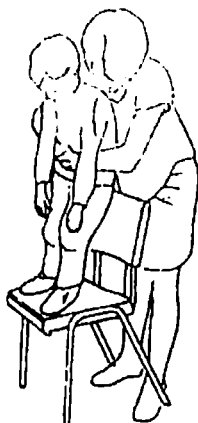
✧ **FBAO relief in the unresponsive / unconscious child**

1. safety.
2. stimulate.
3. shout.
4. Airway-open & check for easily removable foreign body.
5. Breathing-assess & have 5 attempts to deliver at least 2 effective rescuer breaths.
- If ineffective, despite repositioning of the head.*
6. Roll the child onto their side & perform up to 5 back blows.
7. Roll the child into a supine position & perform up to 5 chest thrusts.
8. Airway-open & check for easily removable foreign body.
9. Breathing-assess & have up to 5 attempts to deliver at least 2 effective rescuer breaths.

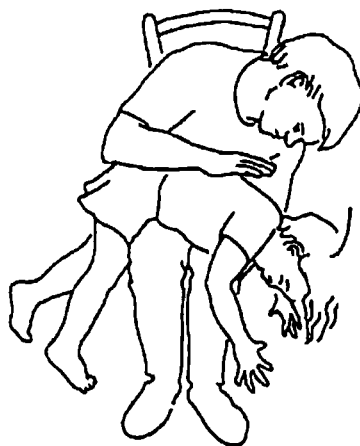
If ineffective, continue with steps 6-9.

- 10- Roll the child onto their side & perform up to 5 back blows.
- 11- Roll the child onto a supine position & perform up to 5 abdominal thrusts.
- 12- Airway-open & check for removable foreign body.
- 13- Breathing-assess & have up to 5 attempts to deliver at least 2 effective rescuer breaths.

Once attempts of rescue breaths are effective, the rest of the child BLS sequence be continued.



Heimlich maneuver in a standing child

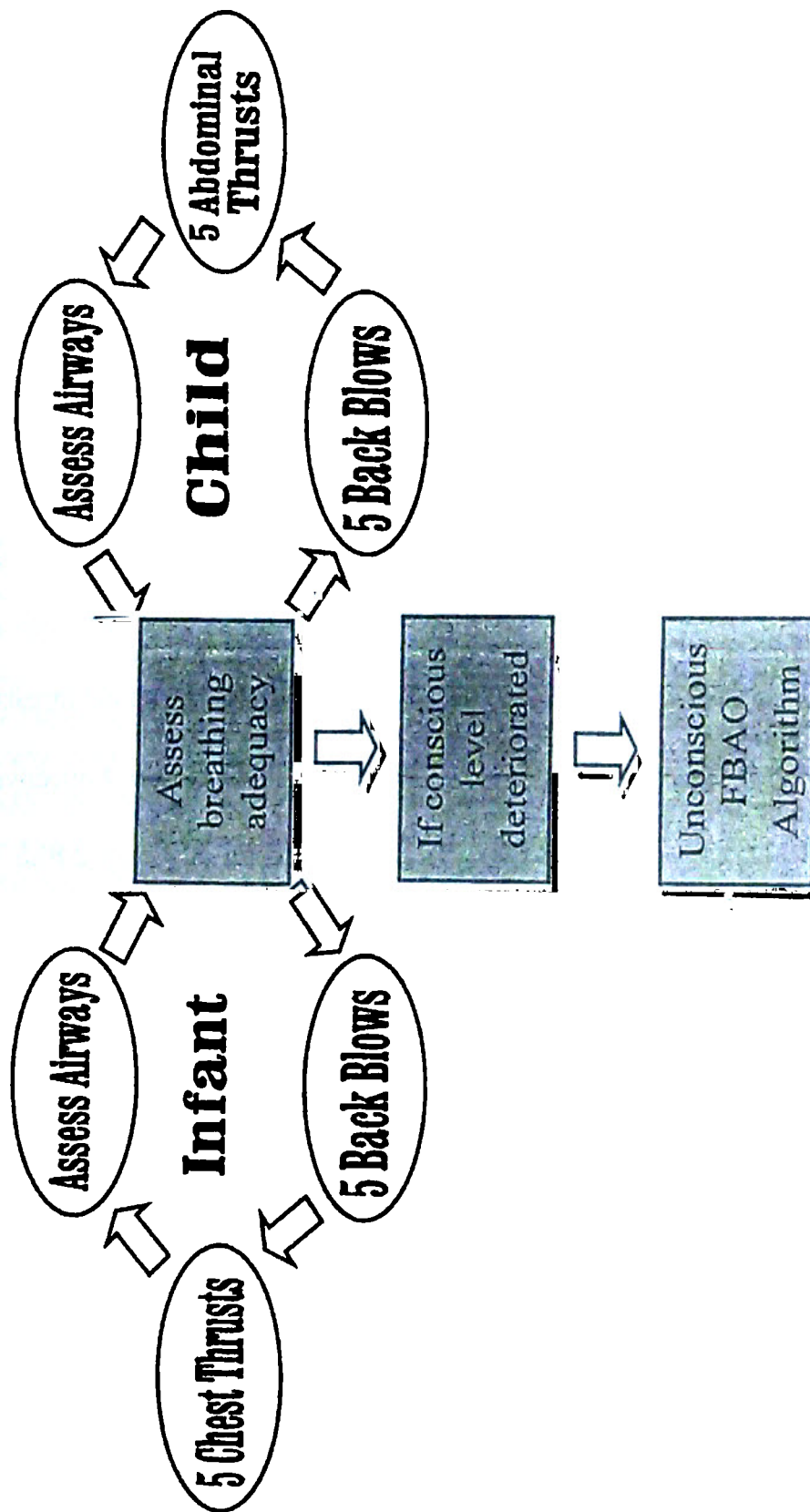


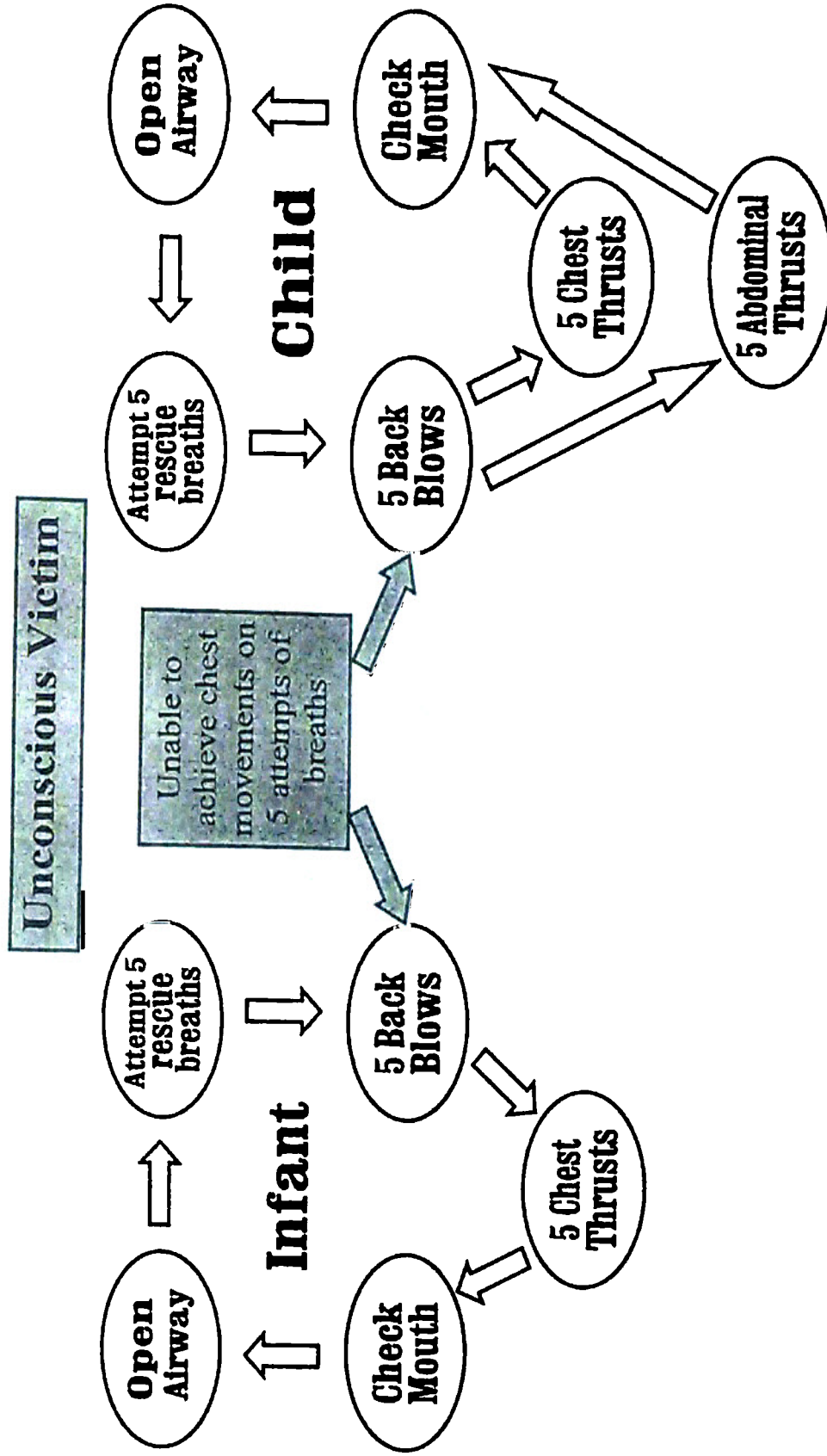
Back blows in a small child



Abdominal thrusts

Conscious Victim





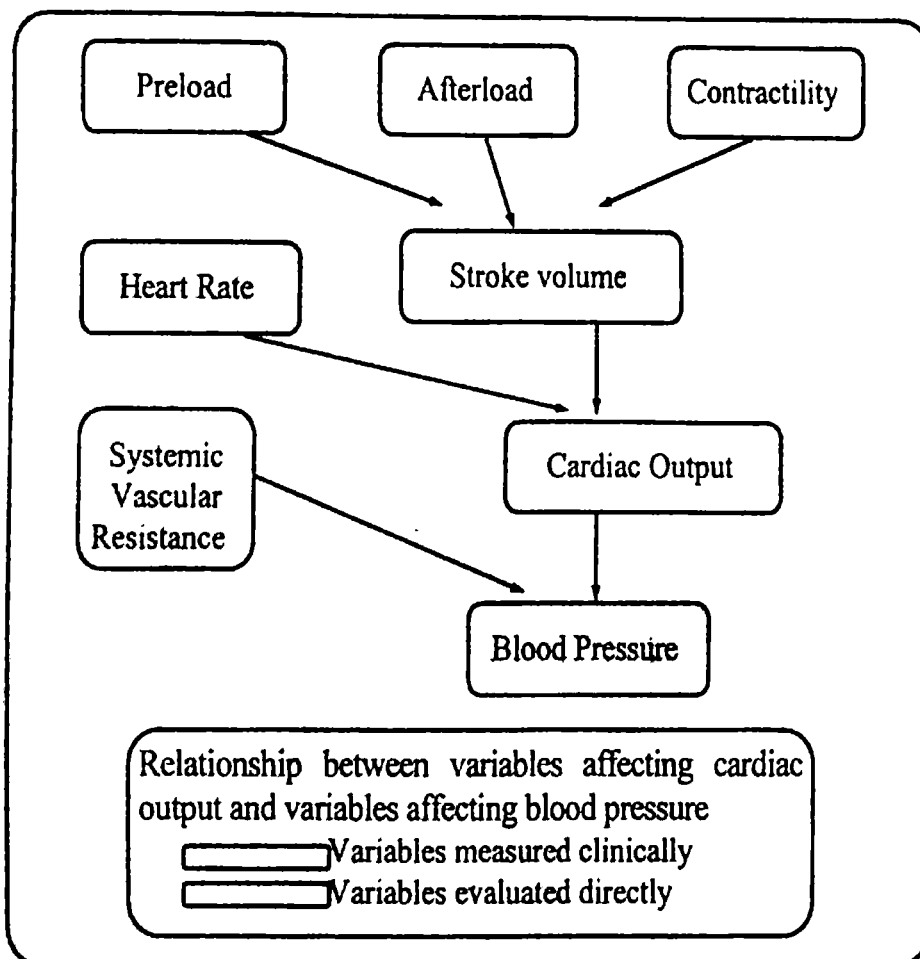
Shock

Recognition of shock by evaluation of circulation function

Shock

- Shock is a clinical state in which blood flow and delivery of tissue nutrients do not meet metabolic demand. Failure to adequately deliver metabolic substances (oxygen, glucose...) and to remove cellular metabolites will lead to anaerobic metabolism, accumulation of lactic acid and cell injury.
- Shock may occur with increased, normal or decreased cardiac output or blood pressure. Shock may be described as being compensated or decompensated.
- **Compensated shock** is the early phase of shock, without hypotension. Although blood pressure is normal, signs of abnormal perfusion (poor skin perfusion, tachycardia, oliguria) are observed.
- **Decompensated shock** is present when hypotension develops and vital organs (heart, brain) perfusion is compromised.

Cardiovascular relationship



- **Aetiologies of shock:**

⚡ **Hypovolaemic shock** is characterized by decreased circulating volume (preload) e.g. bleeding, dehydration,... **TTT** → volume expanders.

⚡ **Distributive shock** is characterized by inadequate distribution of blood, so that, flow is not appropriate to the metabolic demand of the tissues. It is commonly caused by sepsis or anaphylaxis. **TTT** → of the cause

⚡ **Cardiogenic shock** is the result of a myocardial dysfunction or arrhythmia. **TTT** → inotropic drugs.

⚡ **Obstructive shock** is a type of cardiac dysfunction resulting from an obstruction impeding the filling and/or the ejection of the heart (tension pneumothorax, constrictive pericarditis, cardiac tamponade).
TTT → causal (± surgical intervention).

Management of any child in emergency

An urgent assessment must be made of every child in whom respiratory, circulatory or cardio-respiratory failure is suspected

• Urgent ABC Assessment

Opening of the Airway

- ★ Check the patency and the stability of the airway.

Evaluation of Breathing

- ★ **Respiratory rate**
- ★ **Air entry:**
 - Added sounds (stridor, wheezing)
 - Breath sounds
 - Chest expansion
- ★ **Work of breathing (signs of RD):**
 - Flaring of alae nasi
 - Retraction
 - Use of accessory muscles $\pm$ grunting.
- ★ **Colour:**
 - Cynosis or pallor

Evaluation of Circulation

- ★ **Heart rate**
- ★ **Blood pressure**
- ★ **Peripheral and central pulses**
 - Present / Absent
 - Amplitude
- ★ **Skin perfusion**
 - Capillary refill
 - Temperature (line of coldness)
 - Colour, mottling
- ★ **Brain perfusion**
 - Recognition of the parents
 - Interaction with surroundings
 - Tone
 - Pupil size
- ★ **Renal perfusion**
 - Urine output

CHAPTER (X)

BEHAVIOUR

- * Temperament is the style with which the child interacts with the environment. Temperament is an independent psychological attribute that is expressed as a response to an external stimulus.
- * The influence of temperament is bidirectional. The effect of a particular experience will be influenced by the child's temperament, and the child's temperament will influence the responses of others in the child's environment.
- * The perceptions and expectations of parents must be considered when a child's behavior is evaluated. A child that one parent might describe as hyperactive might not be characterized as such by the other parent.
- * For example, if the parents want and expect their child to be predictable but that is not the child's behavioral style, the parents may perceive the child as being bad or having a behavioral disorder rather than as having a developmental variation.
- * The clinician must recognize that each child brings some intrinsic, biologically based traits to its environment and that such characteristics are neither good nor bad, right nor wrong, normal nor abnormal; they are simply part of the child.

COMMON DEVELOPMENTAL CONCERNS

- * I-COLIC
- * II-SLEEP DISORDERS
- * III-TEMPER TANTRUMS
- * IV- BREATH-HOLDING SPELLS
- * V-FEEDING DISORDERS IN INFANTS & YOUNG CHILDREN
- * VI-ANXITIES AND FEARS

COLIC

- * A colicky infant: is one who is healthy and well fed but cries for more than 3 hours a day, for more than 3 days a week, and for more than 3 weeks—commonly referred to as the rule of threes.
- * Infant colic is characterized by severe and paroxysmal crying that occurs mainly in the late afternoon. The infant's knees are drawn up and its fists are clenched, flatus is expelled, and there is minimal response to attempts at soothing.
- * Although colic has traditionally been attributed to gastrointestinal disturbances, this has never been proved. Colic is a behavioral sign or symptom that begins in the first few weeks of life and peaks at age 2–3 months. In about 30–40% of cases, colic continues into the fourth and fifth months.
- * The important word in this definition is “healthy.” Thus, before the diagnosis of colic can be made, the pediatrician must rule out diseases that might cause crying. With the exception of the few infants who respond to elimination of cow's milk from its own or the mother's diet, there has been little firm evidence of an association of colic with allergic disorders.
- * Gastroesophageal reflux is often suspected as a cause of colicky crying in young infants. Undetected corneal abrasion, urinary tract infection, and unrecognized traumatic injuries including child abuse must be among the physical causes of crying considered in evaluating these infants.

Management of Colic

- 1- Parents may need to be educated about the developmental characteristics of crying behavior and made aware that crying increases normally into the second month and abates by the third to fourth month.
- 2-Parents may need reassurance, based on a complete history and physical examination, that the infant is not sick.
- 3-Medications such as phenobarbital elixir and dicyclomine have been found to be somewhat helpful, but their use is to be discouraged because of the risk of adverse reactions and overdosage. A trial of ranitidine hydrochloride might be of help if gastroesophageal reflux is contributing to the child's discomfort.
- 4-For colicky babies refractory to behavioral management, a trial of changing the feedings, eliminating cow's milk from the formula, or from the mother's diet if she is nursing, may be indicated.

SLEEP DISORDERS

- * Sleep is a complex physiologic process influenced by intrinsic biologic properties, temperament, and environmental conditions.
- * Two major sleep stages have been identified clinically and with the use of polysomnography (electroencephalography, electro-oculography, and electromyography):

1-rapid eye movement (REM) sleep

2- Non- rapid eye movement (NREM) sleep

- * Between 20% and 30% of children experience sleep problems severe enough to cause concern. These problems usually fall into three categories:
 - (1) nighttime attacks (parasomnias),
 - (2) sleeplessness (insomnias or dyssomnias), and
 - (3) excessive sleepiness during the day.

NIGHTMARES

- * Nightmares are frightening dreams during REM sleep, typically followed by awakening, which usually occur in the latter part of the night. The peak occurrence is between ages 3 and 5 years, with an incidence between 25% and 50%. A child who awakens during these episodes is usually alert. He or she can often describe the frightening images, recall the dream, and talk about it during the day.
- * A complete medical and psychosocial history should be obtained and a physical examination performed. A detailed sleep history and diary should be maintained to which both parents contribute. Some clinicians use polysomnography to complete the evaluation.

BREATH-HOLDING SPELLS

- * Breath-holding spells are categorized as either cyanotic or pallid.
- * Cyanotic breath-holding spells, the most common type, usually occur in response to anger or frustration. A child's skin typically turns red or blue-purple.
- * Pallid breath-holding spells produce a pale appearance to a child's skin. These spells usually occur in response to fear, pain, or injury, especially after an unexpected blow to the head.
- * In general, breath-holding spells cause a child to faint and may sometimes cause the muscles to twitch or the body to stiffen.

Specific symptoms of cyanotic spells include:

- * A short burst of rigorous crying lasting less than 30 seconds.
- * Hyperventilating (overbreathing).
- * A pause in breathing after exhaling.
- * Red or blue-purple skin color, especially around the lips.

Specific symptoms of pallid spells include:

- * A single cry or no cry at all.
- * Slowing of the heart.
- * Pale skin color.
- * Sweating.
- * Sleepiness or fatigue after the episode.

Cyanotic spells are treated by reassuring the parents , iron therapy and piracetam in resistant cases.

FEEDING DISORDERS IN INFANTS & YOUNG CHILDREN

- * The stages through which the child normally progresses are establishment of homeostasis (0–2 months), attachment (2–6 months), and separation and individuation (6 months to 3 years).
- * During the first stage, feeding can be accomplished most easily when the parent allows the infant to determine the timing, amount, pacing, and preference of food intake.
- * During the attachment phase, allowing the infant to control the feeding permits the parent to engage the infant in a positive manner.
- * When a disturbance occurs in the parent-child relationship at any of these developmental levels, difficulty in feeding may ensue, with both the parent and the child contributing to the dysfunctional interaction.
- * One of the most striking manifestations of food refusal occurs during the stage of separation and individuation. Conflict may arise if the parent seeks to dominate the child by controlling feeding behavior at the same time the child is striving to achieve autonomy. The scenario then observed is of the parent forcing food on the child while the child refuses to eat. This often leads to extreme parental frustration and anger, and the child may be inadequately nourished and developmentally and emotionally thwarted.
- * Children have feeding problems for various reasons. The common denominator, however, is usually food refusal. Infants and young children may refuse to eat if they find eating painful or frightening or have unpleasant food experience.

Factors that aggravate feeding refusal:

- 1-The infant may refuse to eat if the rhythm of the feeding experience with the caregiver is not harmonious.
- 2-The child who has had an esophageal atresia repair and has a stricture may find eating uncomfortable.
- 3-The very young infant with severe oral candidiasis may refuse to eat because of pain.
- 4- The child who has had a choking experience associated with feeding may be terrified to eat (oral motor dysfunction or aspiration).
- 5- The child who is forced to eat by a maltreating parent or an overzealous caregiver may refuse feeds.
- 6-Children who have required nasogastric feedings or who have required periods of fasting and intravenous nutrition in the first 1–2 months of life are more likely to display food refusal behavior upon introduction of oral feedings.

Management of Feeding Disorders

- * The goals of management of the child with poor weight gain are to establish a normal pattern of weight gain and to establish better family functioning.
- * The goal of intervention is to identify factors contributing to the disturbance and to work to overcome them. The parents may be encouraged to view the child's behavior differently and try not to impose their expectations and desires. Alternatively, the child's behavior may need to be modified so that the parents can provide adequate nutrition.
- * When the chief complaint is failure to gain weight, a different approach is required. The differential diagnosis should include not only food refusal but also medical disorders and maltreatment. The most common reason for failure to gain weight is inadequate caloric intake. Excessive weight loss may be due to vomiting or diarrhea, to malabsorption, or to a combination of these factors. In this situation more extensive diagnostic evaluation may be needed.
- * Because of the complexity of the problem, a team approach to the diagnosis and treatment of failure to thrive may be most appropriate. The team should include a physician, nurse, social worker, and dietitian. Occupational and physical therapists, developmentalists, and psychologists may be required.

ANXIETIES AND FEARS

- * Anxiety is defined as "apprehension without apparent cause." It usually occurs when there's no immediate threat to a person's safety or well being, but the threat feels real.
- * Anxiety makes someone want to escape the situation -- fast. The heart beats quickly, the body might begin to perspire, and "butterflies" in the stomach soon follow. However, a little bit of anxiety can actually help people stay alert and focused.
- * Having fears or anxieties about certain things can also be helpful because it makes kids behave in a safe way. For example, a kid with a fear of fire would avoid playing with matches.

The nature of anxieties and fears change as kids grow and develop:

- * Babies experience stranger anxiety, clinging to parents when confronted by people they don't recognize.
- * Toddlers around 10 to 18 months old experience separation anxiety, becoming emotionally distressed when one or both parents leave.
- * Kids ages 4 through 6 years have anxiety about things that aren't based in reality, such as fears of monsters and ghosts.
- * Kids ages 7 through 12 years often have fears that reflect real circumstances that may happen to them, such as bodily injury and natural disaster.
- * As kids grow, one fear may disappear or replace another. For example, a child who couldn't sleep with the light off at age 5 may enjoy a ghost story years later. And some fears may extend only to one particular kind of stimulus. In other words, a child may want to pet a lion at the zoo but wouldn't dream of going near the neighbor's dog.

Some signs that a child may be anxious about something may include:

- * becoming clingy, impulsive, or distracted
- * nervous movements, such as temporary twitches
- * problems getting to sleep and/or staying asleep longer than usual
- * sweaty hands
- * accelerated heart rate and breathing
- * nausea
- * headaches
- * stomachaches

PEDIATRIC ETHICS

- * Pediatric ethics is a branch of bioethics that analyzes moral aspects of decisions made relating to the health care of children. In general terms, the autonomy driven framework of adult medical ethics is replaced by a beneficent paternalism (or parentalism) in pediatrics. Pediatric ethics is distinctive because the pediatric clinician has an independent fiduciary obligation to act in a younger child's best interest that takes moral precedence over the wishes of the child's parent(s).

ASSENT AND PARENTAL PERMISSION

- * The doctrine of informed consent has limited direct application to children and adolescents who lack decisional capacity. The capacity for informed decision-making in health care involves the ability to understand and communicate, to reason and deliberate, and to analyze conflicting elements of a decision using a set of personal values.
- * In contrast to decisions about one's own care, a parent's right to direct a child's medical care is more limited. For this reason, the term parental consent is misleading. The concept of parental permission (rather than consent) reflects a surrogate or proxy decision made by a parent on behalf of a child. It is constrained both by the child's best interest and the independent obligation of clinicians to act in the child's best interest, even if this places them in conflict with a parent.
- * Respect for children must account for both a child's vulnerability and developing capacity. This respect encompasses both the protective role of parental permission and the developmental role of child assent (the child's affirmative agreement). Understanding the concept of assent is one of the major conceptual challenges in pediatric ethics. The dissent (or disagreement) of a child is the opposite of assent and is also morally relevant. Pediatric ethics requires clinicians and parents to override a child's dissent when a proposed intervention is essential to his or her welfare.
- * Older children or adolescents may have the cognitive and emotional capacity to fully participate in health care decisions. If so, the adolescent should be provided with the same information as would be given to an adult patient. In cases like this, the patient may be able to provide informed consent ethically but not legally. The adolescent's parent(s) remain in a guiding and protective role. The process of communication and negotiation will be more complex should disagreement arise between the parent and adolescent

TREATMENT OF CRITICALLY ILL CHILDREN

- * Infants, children, and adolescents who become critically ill may recover fully, may die, or may survive with new or worsened limitations of function. Uncertainty about outcomes can make planning goals of care difficult, or if misunderstandings between patient, families, and medical staff occur, may drive conflict over treatment proposals. Ethical issues that arise during critical illness include balancing benefits, burdens, and harms of therapy in the face of uncertainty; maintaining a helpful degree of transparency and communication about medical standards of care at an institution.

DEATH BY NEUROLOGIC CRITERIA

- * Death by neurologic criteria (DBNC, commonly referred to as “brain death”) may be difficult for families to understand when the child appears to be breathing (albeit on a ventilator), pink, and warm to the touch, and when language such as “life support” is used at the bedside by staff. Studies have also documented clinician misunderstanding of the diagnosis of DBNC. For these reasons, strict criteria adhering to nationally accepted guidelines must be used to determine when irreversible cessation of brain and brainstem function has occurred, and to adequately document these findings.

RESEARCH

- * The central ethical challenge of pediatric research is the need to balance protection of children from research risk against the ethical imperative of conducting studies to better the lives of future children. Research is defined in the federal regulations as “a systematic investigation designed to develop or contribute to generalizable knowledge.” For any research to be performed, the risks should be minimized and reasonable with respect to any anticipated benefits to the subjects and the importance of the resulting knowledge. The fact that some children derive a direct benefit from participation in research must also be considered, making it important to distinguish research with the prospect of direct benefit from nontherapeutic pediatric research. Because children are a vulnerable population, there are restrictions on the research risks to which a child may be exposed that contrast with the risk level acceptable for research with consenting adults. These restrictions function by limiting the kind of research institutional review boards (IRBs) are permitted to approve and by specifying the conditions under which parent(s) have the moral and legal authority to permit a child to participate in research.

RELIGIOUS OR CULTURAL OBJECTIONS TO TREATMENT

- Differences in religious beliefs or cultural norms may lead to conflict between patients, families, and medical caregivers over the approach to medical care. Pediatricians need to remain sensitive to and maintain an attitude of respect for these differences, yet recognize that an obligation exists to provide effective medical treatment to the child.
- An adult with decision-making capacity is recognized as having the right to refuse treatment on religious or cultural grounds, but children who have not yet developed this capacity are considered a vulnerable population that have a right to treatment. In situations that threaten the life of the child or that may result in substantial harm, legal intervention should be sought if reasonable efforts toward collaborative decision-making are ineffective. If a child's life is imminently threatened, medical intervention is ethically justified despite parental objections.

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